

EXHIBIT A



US008287482B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.:** **US 8,287,482 B2**
(45) **Date of Patent:** **Oct. 16, 2012**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

(75) Inventors: **David Y. Badawi**, Northbrook, IL (US);
Paul Badawi, San Francisco, CA (US)

(73) Assignee: **Sight Sciences, Inc.**, San Francisco, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 305 days.

(21) Appl. No.: **12/695,053**

(22) Filed: **Jan. 27, 2010**

(65) **Prior Publication Data**

US 2010/0191329 A1 Jul. 29, 2010

Related U.S. Application Data

(63) Continuation of application No. 11/475,523, filed on Jun. 26, 2006, now Pat. No. 7,909,789.

(51) **Int. Cl.**

A61M 5/00 (2006.01)

A61F 2/04 (2006.01)

(52) **U.S. Cl.** **604/8**; 604/9; 623/23.64; 623/23.7

(58) **Field of Classification Search** 604/8, 9, 604/264; 623/23.64, 23.7

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,159,161 A	12/1964	Ness
4,068,664 A	1/1978	Sharp et al.
4,457,757 A	7/1984	Molteno
4,936,825 A	6/1990	Ungerleider
4,957,505 A	9/1990	McDonald
5,486,165 A	1/1996	Stegmann

5,569,197 A	10/1996	Helmus et al.
5,626,558 A	5/1997	Suson
5,639,278 A	6/1997	Dereume et al.
5,868,697 A	2/1999	Richter et al.
6,050,970 A	4/2000	Baerveldt
6,375,642 B1	4/2002	Grieshaber et al.
6,494,857 B1 *	12/2002	Neuhann 604/8
6,508,779 B1	1/2003	Suson
6,616,996 B1	9/2003	Keith et al.
7,207,980 B2	4/2007	Christian et al.

(Continued)

FOREIGN PATENT DOCUMENTS

WO WO-00/64393 A1 11/2000

(Continued)

OTHER PUBLICATIONS

Boyle, E.L. (Feb. 1, 2006). "New Glaucoma Devices Take Different Approaches to IOP Lowering," *Ocular Surgery News U.S. Edition*, located at <<http://www.osnsupersite.com/view.aspx?rid=12436>>, last visited on Nov. 9, 2009, 6 pages.

(Continued)

Primary Examiner — Leslie Deak

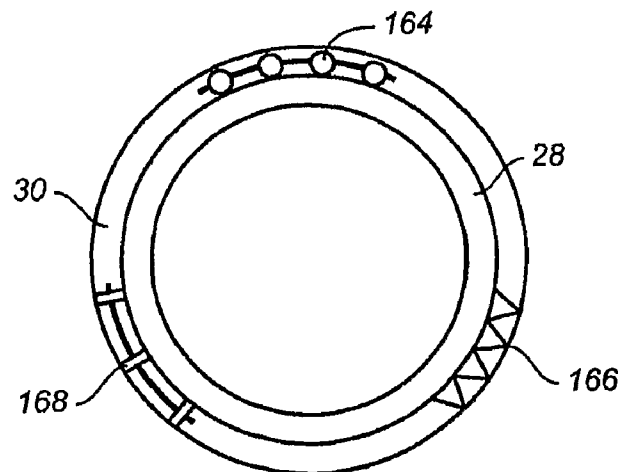
(74) *Attorney, Agent, or Firm* — Morrison & Foerster LLP

(57)

ABSTRACT

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmurial fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmurial fluid flow across the canal.

86 Claims, 15 Drawing Sheets



US 8,287,482 B2

Page 2

U.S. PATENT DOCUMENTS

7,909,789	B2	3/2011	Badawi et al.	
7,951,155	B2	5/2011	Smedley et al.	
7,967,772	B2	6/2011	Mckenzie et al.	
8,075,511	B2	12/2011	Tu et al.	
2002/0013546	A1	1/2002	Grieshaber et al.	
2002/0133168	A1	9/2002	Smedley et al.	
2004/0193262	A1*	9/2004	Shadduck	623/4.1
2004/0254521	A1	12/2004	Simon	
2004/0260228	A1	12/2004	Lynch et al.	
2005/0267555	A1	12/2005	Marnfeldt et al.	
2006/0069340	A1	3/2006	Simon	
2006/0195187	A1*	8/2006	Stegmann et al.	623/4.1
2007/0298068	A1	12/2007	Badawi et al.	
2009/0132040	A1	5/2009	Frion et al.	
2009/0227934	A1	9/2009	Euteneuer et al.	
2011/0098809	A1	4/2011	Wardle et al.	
2011/0130831	A1	6/2011	Badawi et al.	
2011/0196487	A1	8/2011	Badawi et al.	
2012/0059461	A1	3/2012	Badawi et al.	

FOREIGN PATENT DOCUMENTS

WO	WO-2005/105197	A2	11/2005
WO	WO-2005/105197	A3	11/2005
WO	WO-2006/066103	A2	6/2006
WO	WO-2006/066103	A3	6/2006

OTHER PUBLICATIONS

Final Office Action mailed on Nov. 1, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 12 pages.

International Search Report mailed on Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, five pages.

International Search Report mailed on Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 2 pages.

Non-Final Office Action mailed on May 17, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 10 pages.

Non-Final Office Action mailed on Mar. 15, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 4 pages.

Restriction Requirement mailed on Sep. 30, 2009, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 9 pages.

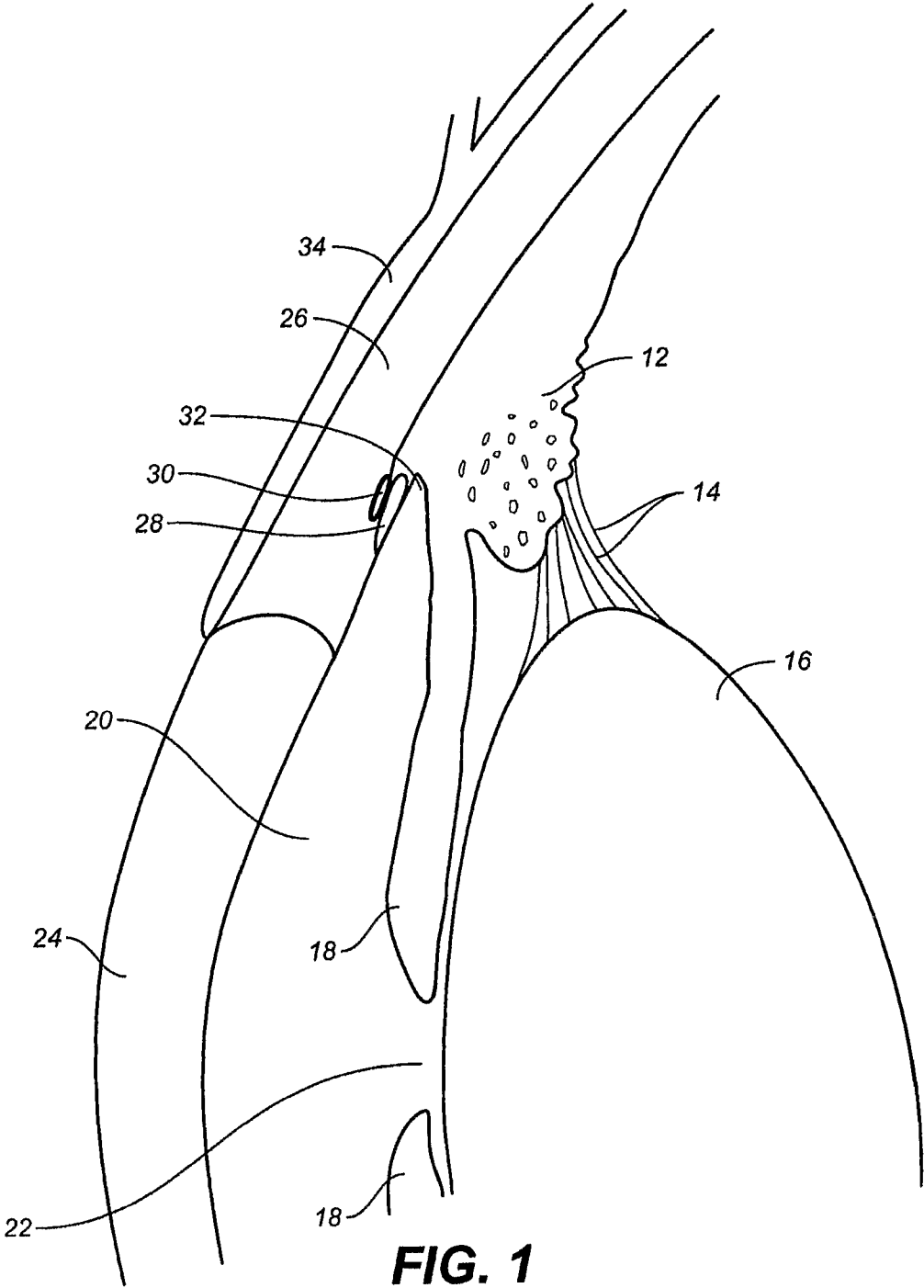
Restriction Requirement mailed on Feb. 23, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 6 pages.

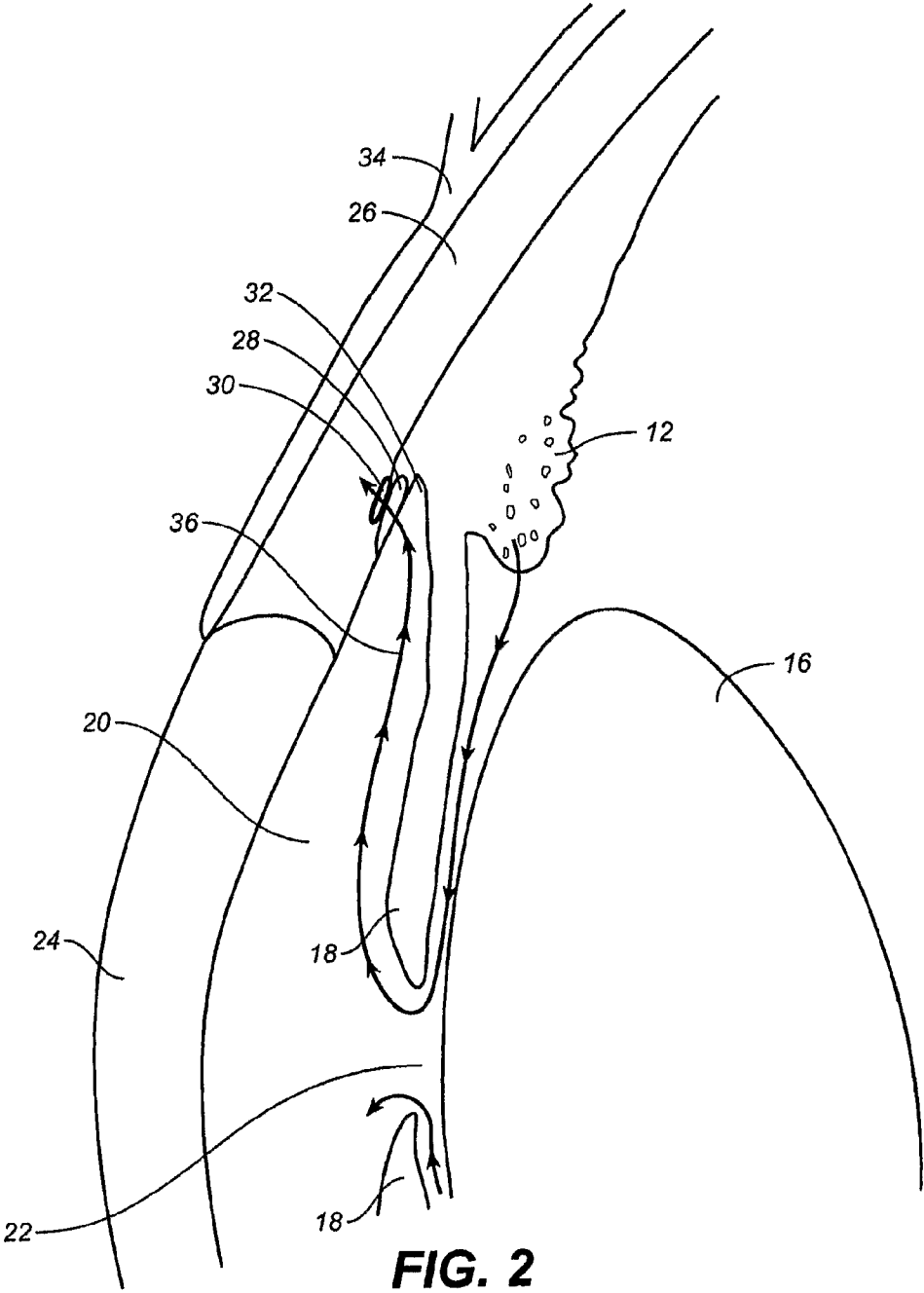
Restriction Requirement mailed on Mar. 28, 2012, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 7 pages.

Written Opinion mailed on Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, 6 pages.

Written Opinion mailed on Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 5 pages.

* cited by examiner





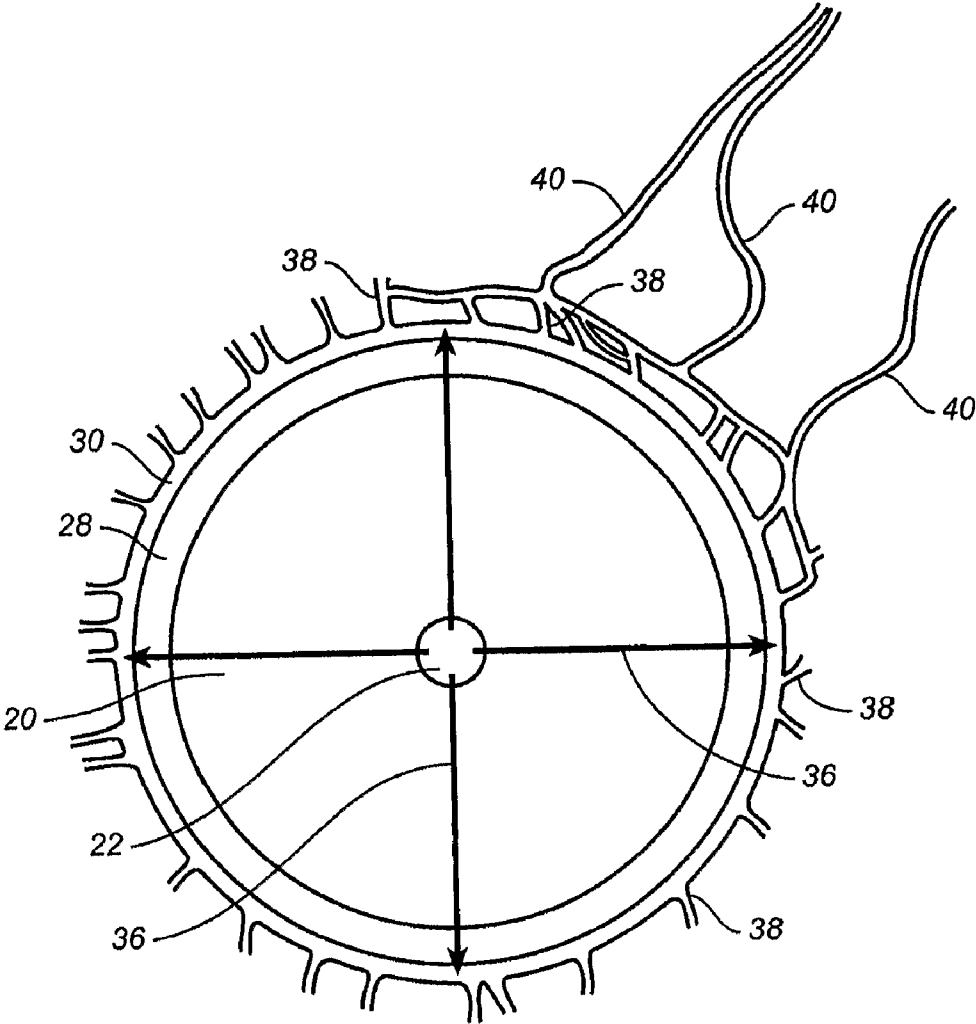


FIG. 3

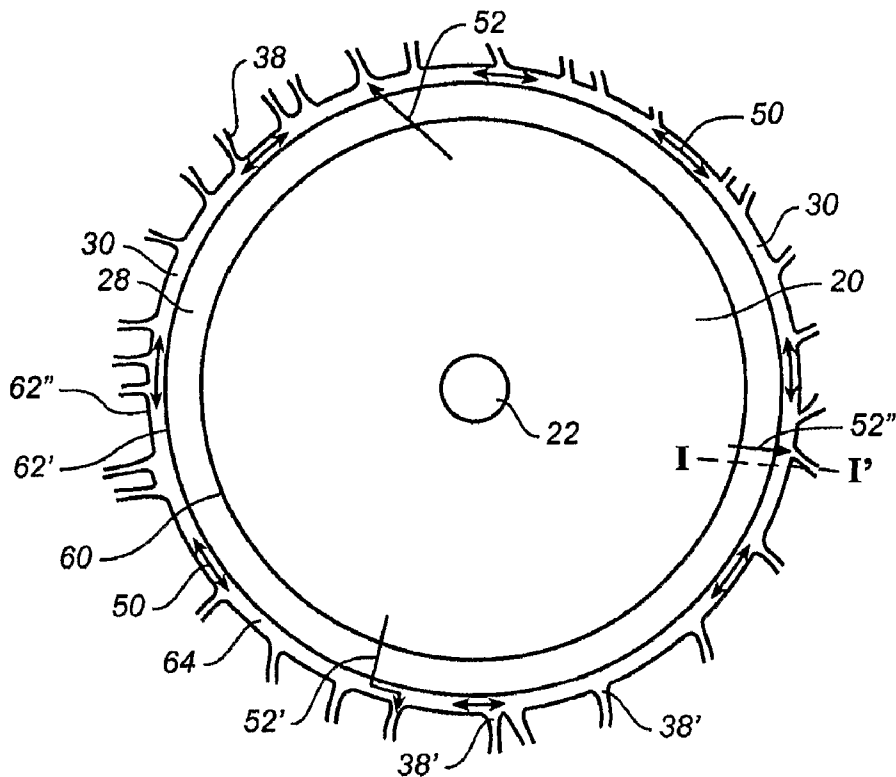


FIG. 4A

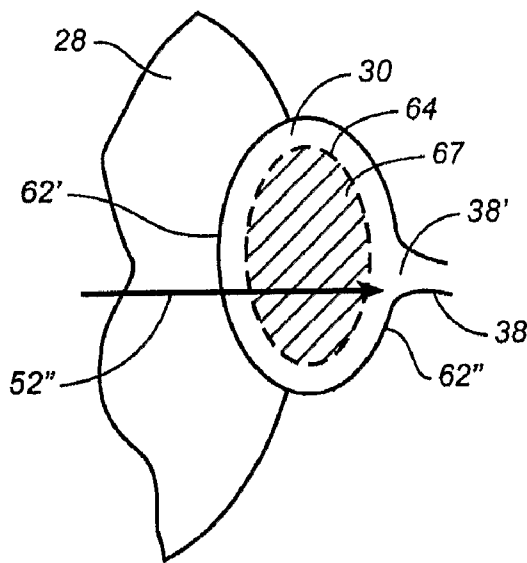


FIG. 4B

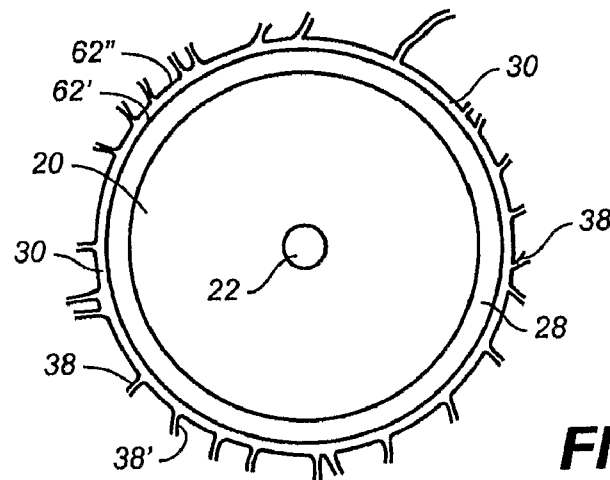


FIG. 5A

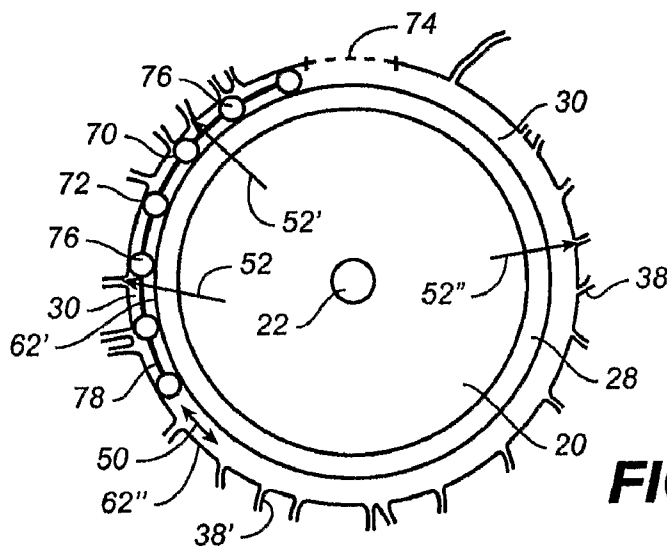


FIG. 5B

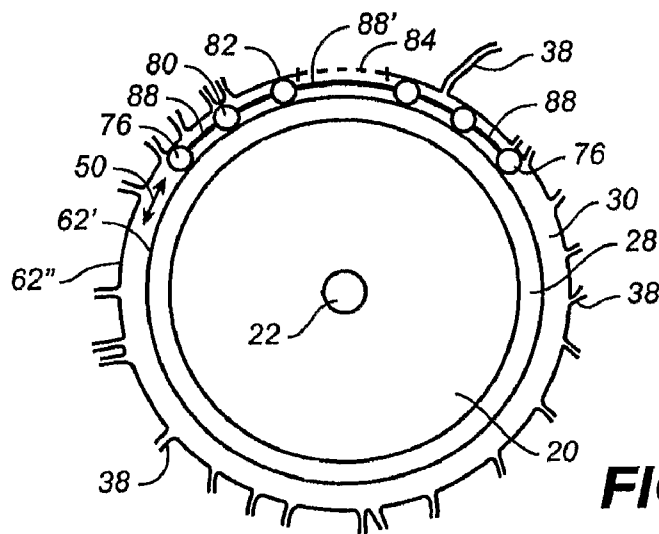


FIG. 5C

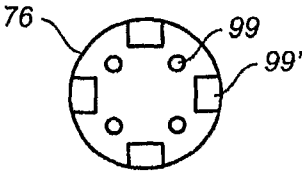
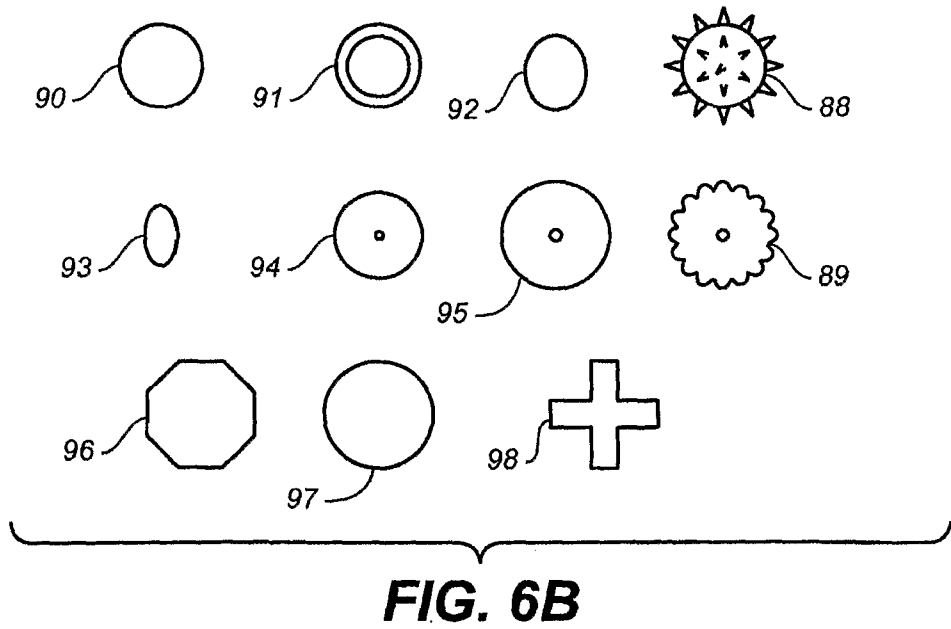
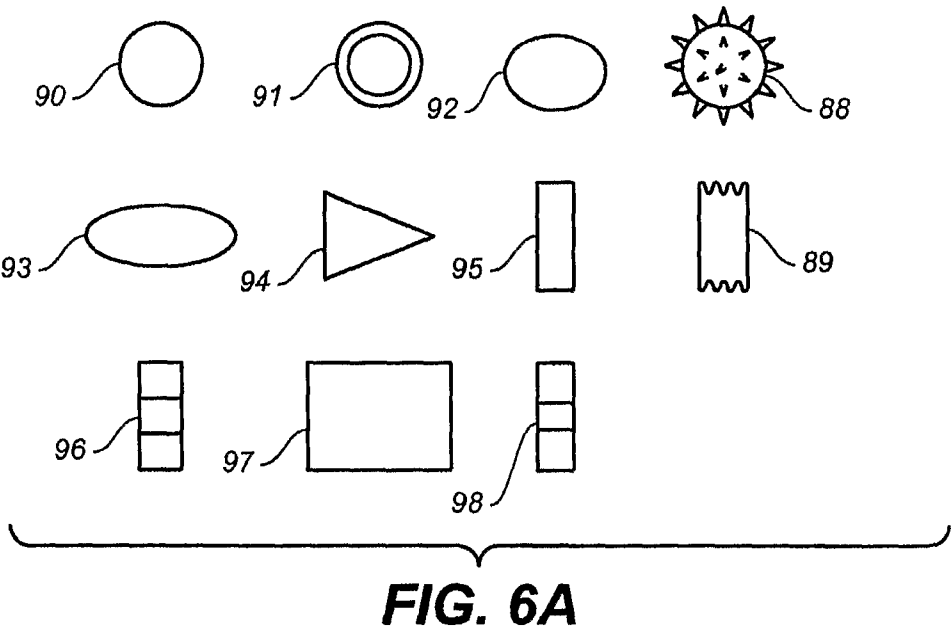


FIG. 6C



FIG. 7A



FIG. 7B

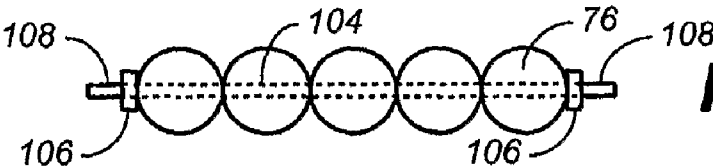


FIG. 7C

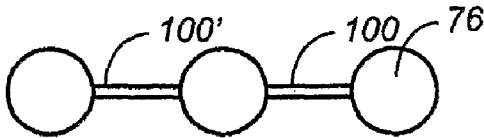


FIG. 7D

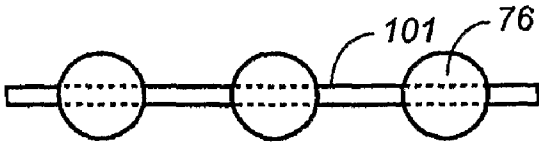


FIG. 7E

U.S. Patent

Oct. 16, 2012

Sheet 8 of 15

US 8,287,482 B2

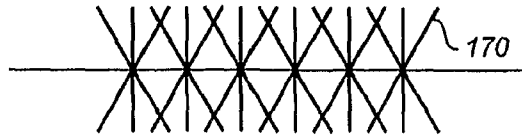


FIG. 8A

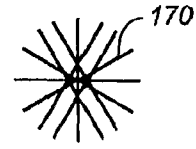


FIG. 8B

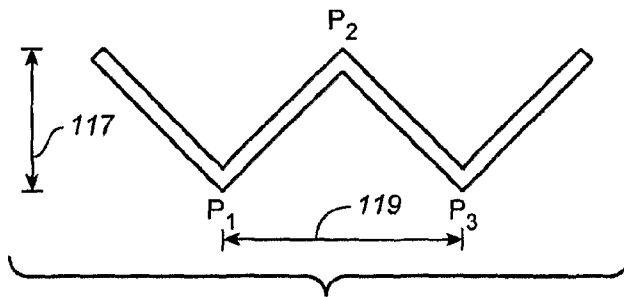


FIG. 8C



FIG. 8D

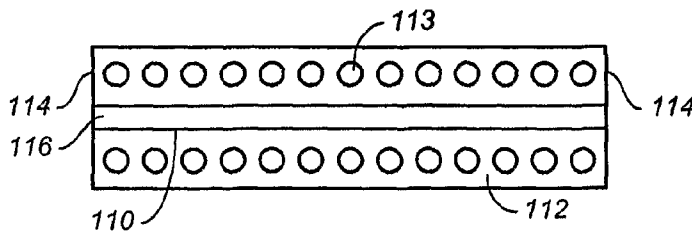


FIG. 8E

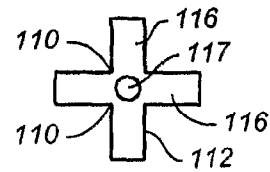


FIG. 8F

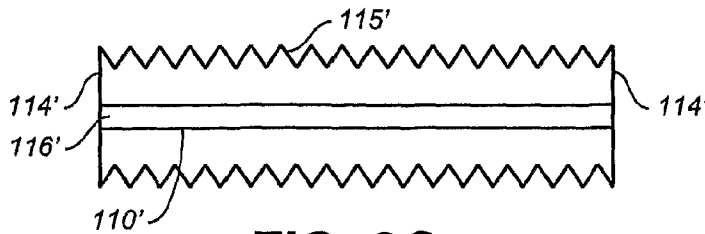


FIG. 8G

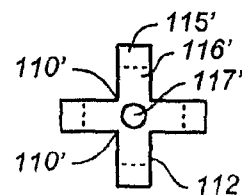
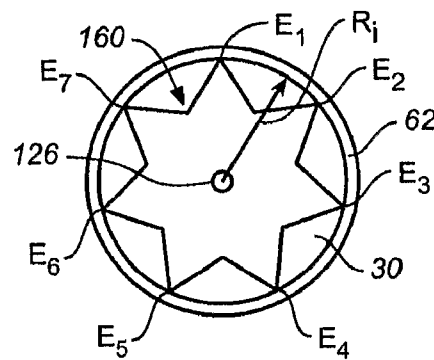
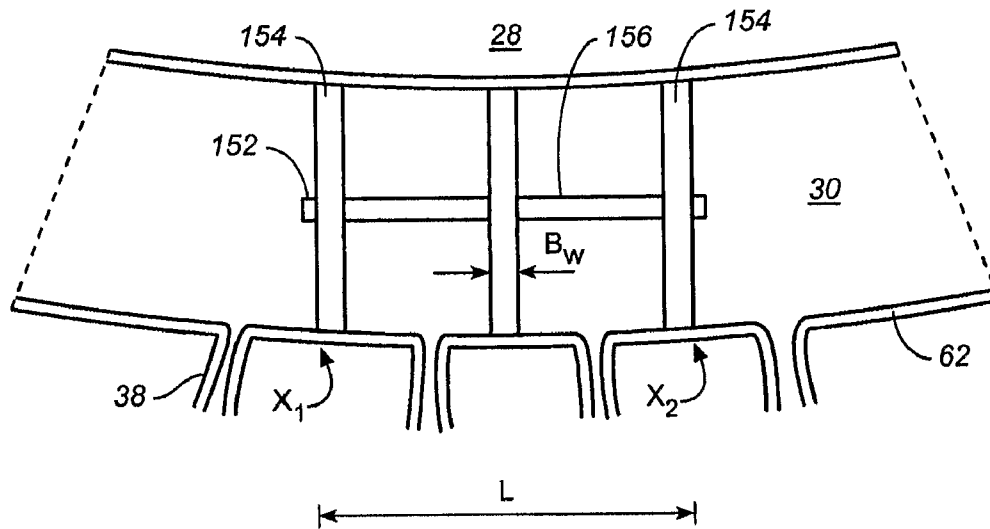


FIG. 8H



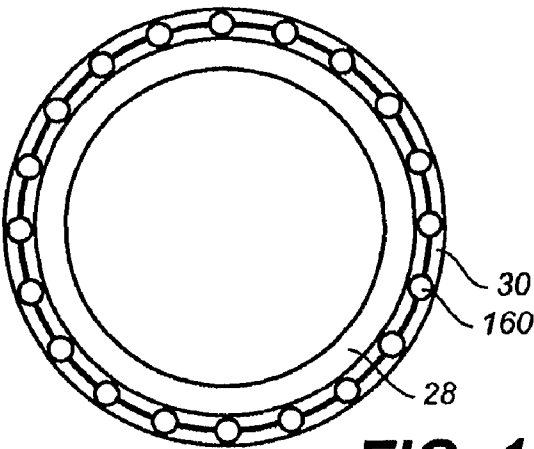


FIG. 10A

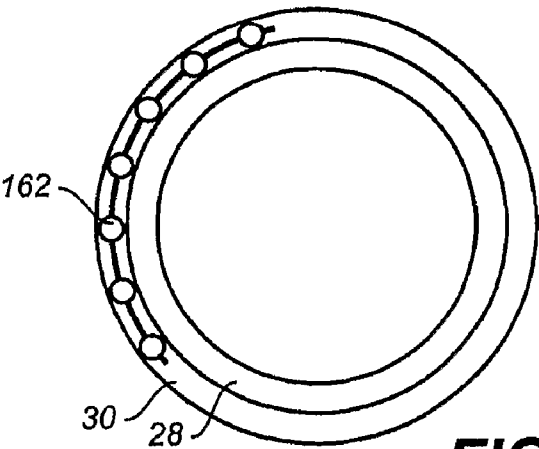


FIG. 10B

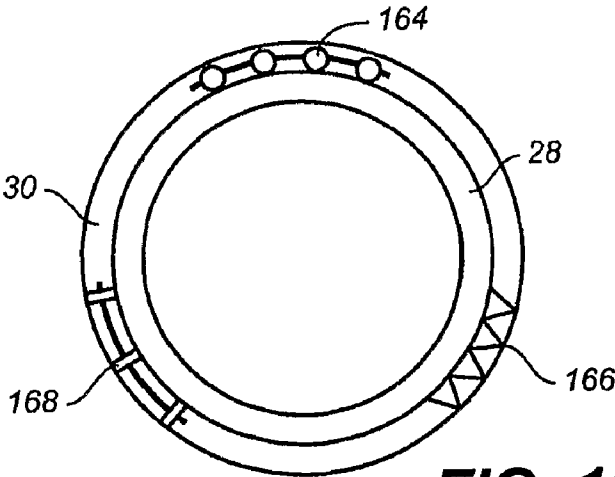


FIG. 10C

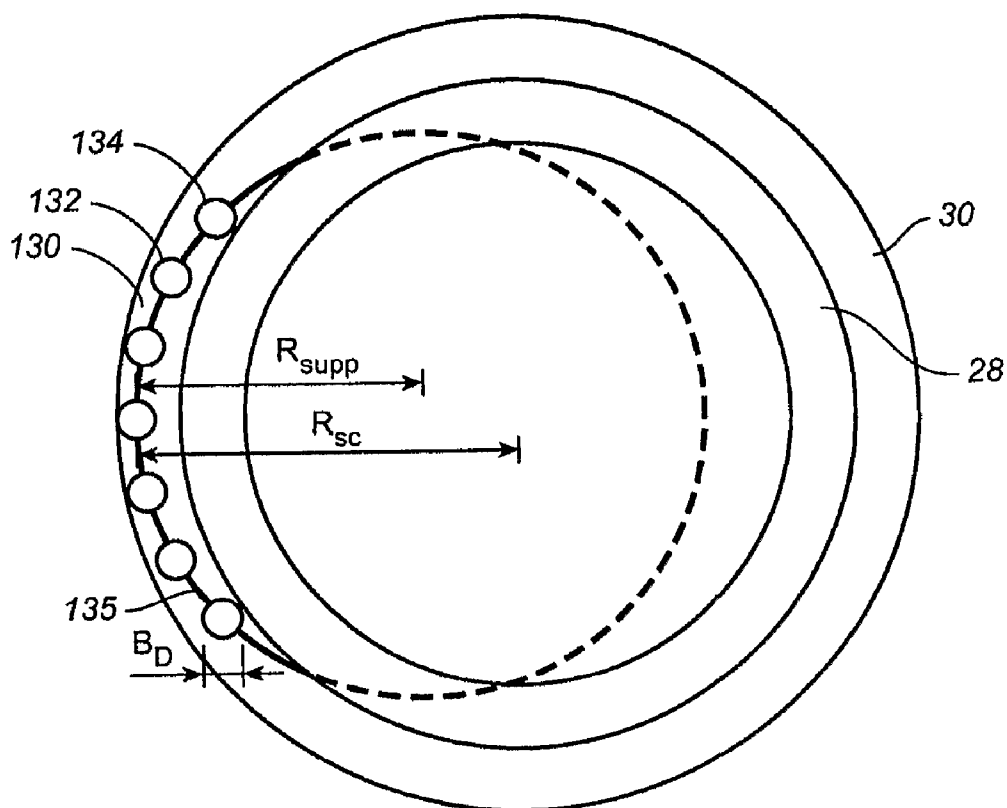


FIG. 11A

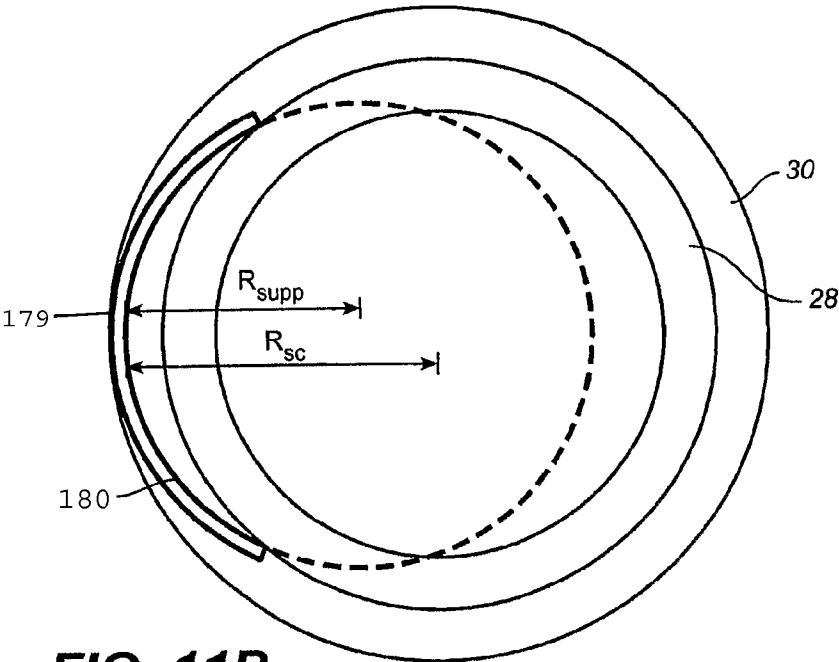


FIG. 11B

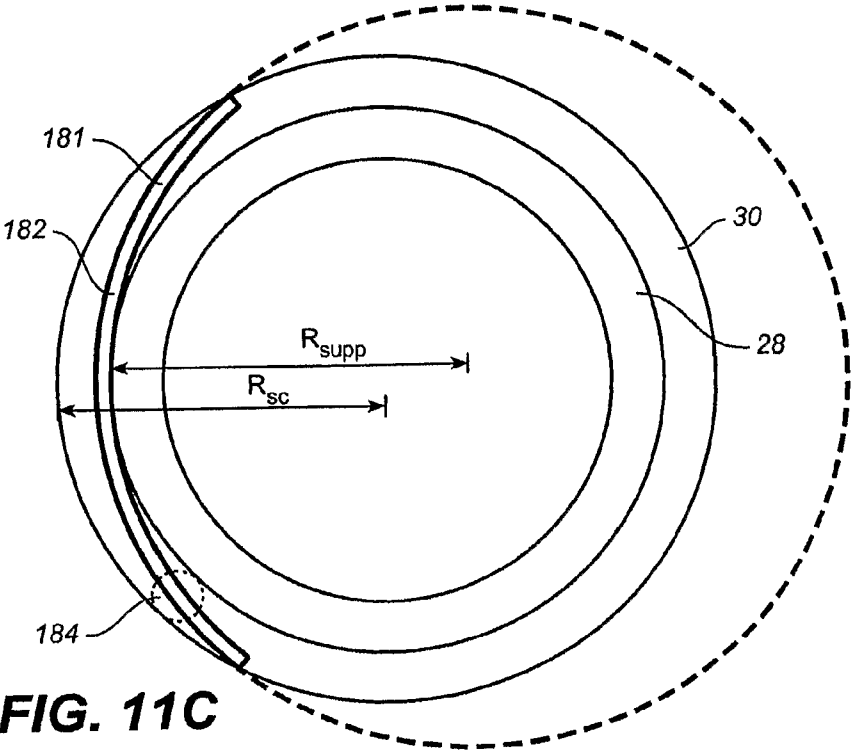


FIG. 11C

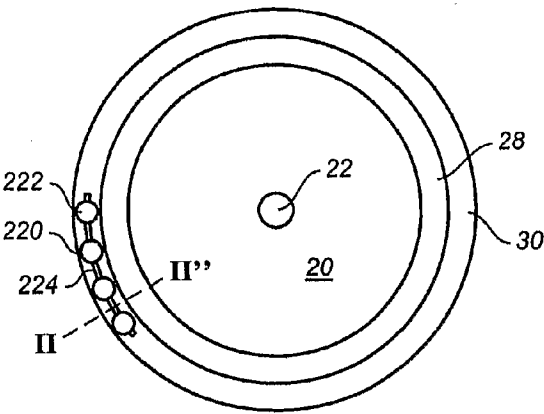


FIG. 12A

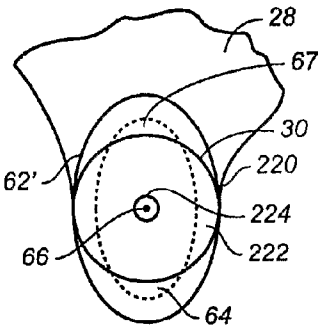


FIG. 12B

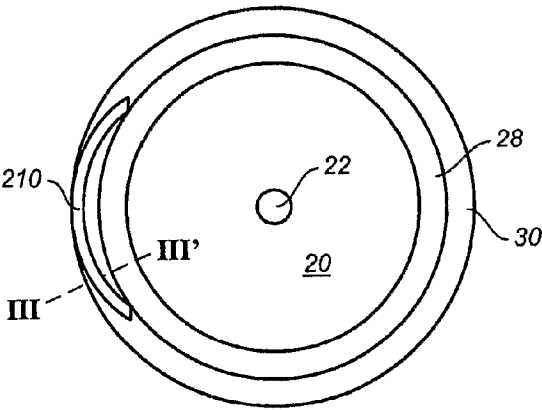


FIG. 12C

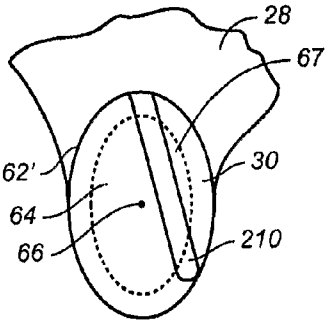


FIG. 12D

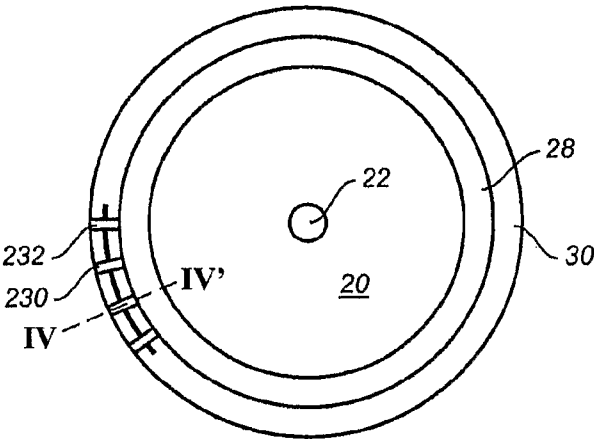


FIG. 12E

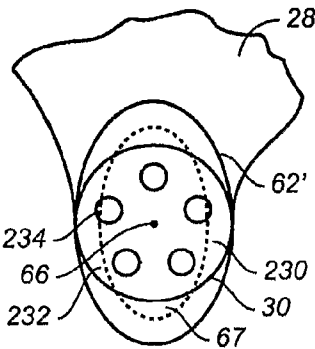


FIG. 12F

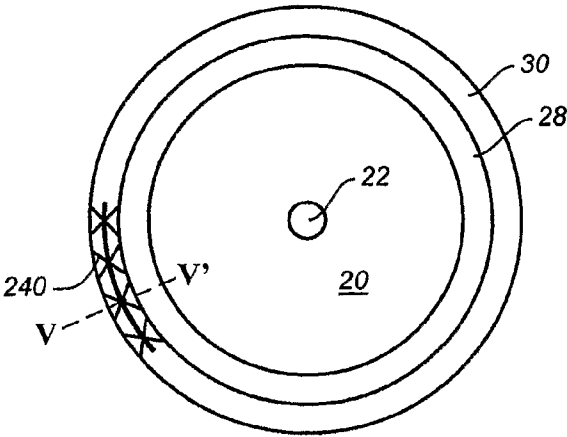


FIG. 12G

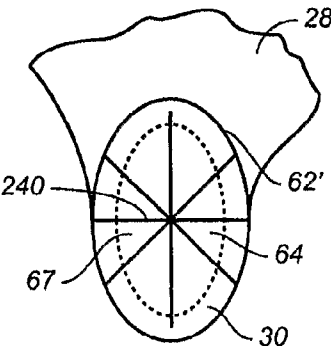


FIG. 12H

U.S. Patent

Oct. 16, 2012

Sheet 15 of 15

US 8,287,482 B2

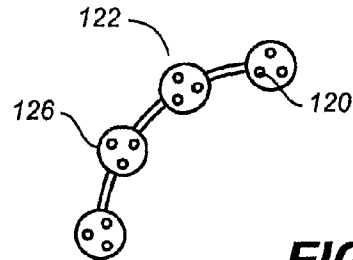


FIG. 13

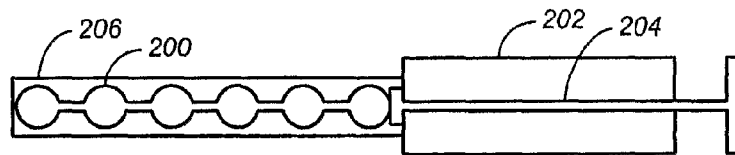


FIG. 14A

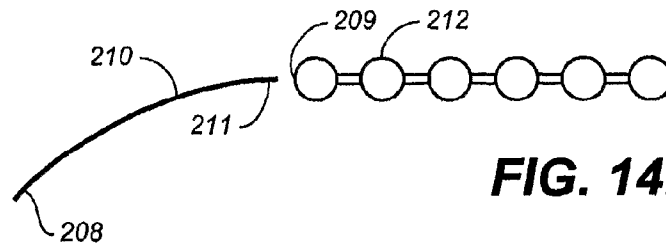


FIG. 14B



FIG. 14C

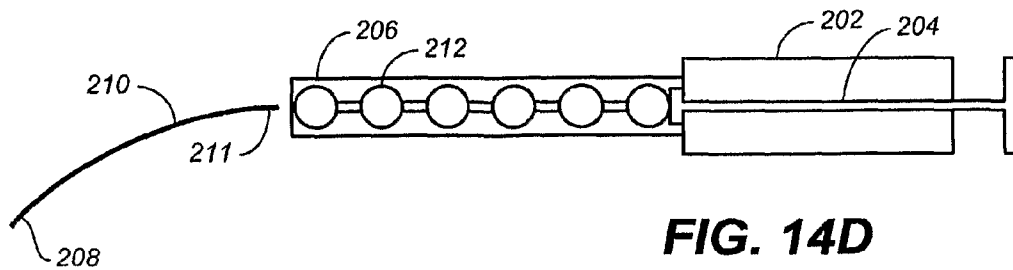


FIG. 14D

US 8,287,482 B2

1

INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 11/475,523, filed on Jun. 26, 2006, the disclosure of which is incorporated herein by reference in its entirety

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical

2

systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjunctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmurial flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal. The support does not substantially interfere with transmurial flow across Schlemm's canal, and thereby utilizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocom-

US 8,287,482 B2

3

patible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer; a polyorthoester; a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a poly(anhydride); a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a poly(ether-ester); a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, cubical, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted between three beads, the connectors may be of the same or different lengths. The connectors can include the same or different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include

4

fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmurial flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can include implanting at least two supports. If more than one support is implanted within a single eye, the multiple supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In

US 8,287,482 B2

5

other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 provides a partial cross-sectional side view of a normal human eye.

FIG. 2 provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. 3 shows a front view of normal fluid drainage from the eye.

FIG. 4A shows an alternative front view of normal fluid drainage paths from the eye. FIG. 4B shows a cross-sectional view along line I-I'.

FIG. 5A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. 5B shows a front view of a device including a support inserted into Schlemm's canal that allows transmurial flow across the canal. FIG. 5C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmurial flow across the canal.

FIG. 6A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. 6B shows the corresponding front views of the element or bead configurations shown in FIG. 6A. FIG. 6C illustrates an element or bead having fenestrations.

FIG. 7A illustrates a support having multiple juxtaposed beads. FIG. 7B illustrates a support having multiple juxtaposed and connected beads. FIG. 7C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. 7D shows a support having multiple, spaced-apart but connected beads. FIG. 7E illustrates beads threaded onto a connector.

FIGS. 8A-B show side and front views, respectively, of a support having an open network structure. FIGS. 8C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at least three points (labeled P₁, P₂, P₃). FIGS. 8E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. 8G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. 9A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. 10A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. 11A-B illustrate two configurations of supports having a smaller radius of curvature than Schlemm's canal. FIG. 11C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. 12A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. 12B shows a cross-sectional view along line II-II'. FIG. 12C illustrates a variation of a support traversing the central core of the canal. FIG. 12D shows a cross-sectional view along line III-III'. FIG. 12E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. 12F shows a cross-sectional view along line IV-IV'. FIG. 12G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. 12H shows a cross-sectional view along line V-V'.

6

FIG. 13 shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. 14A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. 14B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. 14C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. 14D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmurial fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. 1 shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body 12 is connected to iris 18 and to lens 16 via zonular fibrils 14. The anterior chamber of the eye 20 is bounded on its anterior (front) surface by cornea 24. In the center of iris 18 is pupil 22. Cornea 24 is connected on its periphery to sclera 26, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork 28 is located on the outer peripheral surface of anterior chamber 20. The trabecular meshwork extends 360° circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork 28 is Schlemm's canal 30. Schlemm's canal extends 360° circumferentially around the trabecular meshwork. At the apex formed between iris 18, meshwork 28 and sclera 26 is angle 32. Conjunctiva 34 is a membrane overlaying sclera 26 and lining the inside of the eyelid (not shown).

FIG. 2 shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body 12 and its path through and out of the eye is indicated by solid directional line 36. The aqueous humor flows from ciliary body 12, between lens 16 and iris 18, through pupil 22 into anterior chamber 20, across trabecular meshwork 28, across Schlemm's canal 30, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. 3 shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber 20 via pupil 22. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines 36. The fluid crosses trabecular meshwork 28 and traverses Schlemm's canal 30 to reach aqueous veins or collector channels 38. There are typically 25-30 collector channels located in a human eye. Collector channels 38 are connected to vasculature 40, whereby the drained aqueous humor enters the bloodstream. Although the direction of net or bulk fluid flow is depicted as radially outward by directional lines 36 from pupil 22 for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. 4A-B. FIG. 4A shows a front view of an eye, and FIG. 4B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal 30 is depicted by directional lines 50. Fluid that does not traverse canal 30 to reach collector

7

channels **38** may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines **52**, **52'**, and **52''**. In each of these paths, fluid enters trabecular meshwork **28** along its inner peripheral surface **60** and exits the meshwork along its outer peripheral surface **62'**. Meshwork outer peripheral surface **62'** provides the inner peripheral surface or wall of Schlemm's canal **30**. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork **38** through inner peripheral surface or wall **62'** of Schlemm's canal **30** to reach lumen **64** of the canal. Second, fluid must flow from lumen **64** through canal outer peripheral wall **62''** through apertures **38'** to enter collector channels **38**. Finally, the collector channels **38** feed the drained fluid into vasculature. Lumen **64** of canal **30** includes a central core region **67**. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflow from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1) fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral boundary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the connector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's

8

canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. 5A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal **30**, where canal outer peripheral wall **62''** is very close to canal inner peripheral wall **62'**. Although Schlemm's canal **30** is depicted in FIG. 5A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels **38** is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. 5B illustrates an example of a device **70** inserted into Schlemm's canal **30** through incision site **74**. Device **70** in this example is positioned to one side of incision site **74**. Device **70** includes support **72** that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall **62'** and canal outer wall **62''** to reach collector channels **38** via apertures **38'**. In the example shown in FIG. 5B, support **72** includes elements or beads **76** connected with connectors **78**. In this variation, the distance between canal inner wall **62'** and outer wall **62''** is approximately determined by the cross-sectional dimension of support **72**, which is in turn determined by the largest cross-sectional diameter of the beads **76**. Therefore, circumferential (i.e., longitudinal) fluid flow around and along the canal **30** indicated by directional line **50** may be inhibited by the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52''** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters

US 8,287,482 B2

9

(e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. 5C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. 5B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. 6A and 6B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges, **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. 6C, elements or beads **76** may include fenestrations **99, 99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. 6C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. 7A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. 7A), connected and juxtaposed (FIGS. 7B and 7C), or connected together with connectors **100, 100'** to form intervals between beads (FIG. 7D). In addition, beads may be threaded onto a connector **101** (FIG. 7E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. 7B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. 7C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knotting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of

10

external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. 7D, multiple connectors **100, 100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100, 100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100, 100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. 7E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100, 100', 101** can be flexible, such as thin polymer threads or metal wires. Connectors **100, 100', 101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100, 100', 101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. 8A-F. As illustrated in FIG. 8A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. 8A-B will have minimal surface area contact with the walls of Schlemm's canal, i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. 8C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. 8C, the support will contact the wall of Schlemm's canal at least three points, labeled P_1 , P_2 , and P_3 , after implantation. In FIGS. 8E-H, examples of rod-like supports having fluted edges are shown. In FIGS. 8E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include fenestrations **113**. The support can include central bore **117**. In FIGS. 8G-H, fluted edges **110'** extend along sides **112'** to form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. 8E-H, the support may contact the canal walls at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. 8A-B shows, some supports only

US 8,287,482 B2

11

have point contacts with the canal wall. For the supports shown in FIGS. 5B-C, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. 6A-B may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. 7D-E that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. 8C-D, in some variations, the support contacts the interior wall of the canal at least two points; or at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided in FIGS. 9A-B. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder C having length L, extending circumferentially from a first end X_1 to a second end X_2 of support **152**, and inside radius R_i . In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder C as described above. In other variations, the support contacts less than 10% of the surface area of C. In still other variations, the support contacts less than 30% of the surface area of C. For example, the support **152** shown in FIGS. 9A-B contacts the canal wall **62** only at bead outer peripheral edges at E_1 - E_7 , along a distance of the bead width $B_{w'}$. There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmural flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapeable metal having a sinusoidal or zig-zag configuration as shown in FIGS. 8C-D, a cross-sectional dimension **117** of the support can be decreased or increased by applying tension along dimension **119**. As illustrated in FIG. 10A, a support **160** can extend essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately half way around the circumference of the canal (not shown). As shown in FIG. 10B, a support **162** can extend less than half way around the canal. As shown in FIG. 10C, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. 11A, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension B_D . Support **132** comprises a stiff arcuate element **135** with a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal R_{SC} . The

12

smaller, fixed radius of curvature R_{supp} of arcuate member **135** urges canal **30** to open more than B_D . In another variation shown in FIG. 11B, support **179** comprises an arcuate member **180** without beads having a radius of curvature R_{supp} that is less than the radius of curvature R_{SC} of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. 11C, support **181** comprises an arcuate member **182** having a radius of curvature R_{supp} larger than that of Schlemm's canal R_{SC} . Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. 11C, support **181** can include beads **184**. To urge open the canal, the radius of curvature R_{supp} of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal R_{SC} . For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member R_{supp} in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature R_{supp} of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at least one point. Referring to FIG. 12A, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. 12B shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. 12C, a front view of an arcuate support **210** is shown. FIG. 12D shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. 12E, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. 12F. As illustrated in FIG. 12F, bead **232** with fenestrations **234** occupies the majority of central core **67** of canal **30**. In other variations, the support occupies only a small portion of the central core of the canal. For example, in FIG. 12G, a front view of a support **240** having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. 12H.

A support can be made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacrylate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives,

US 8,287,482 B2

13

flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly(lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly(ethylene glycol) copolymer, a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer, a poly(lactic acid)/poly(ethylene glycol) copolymer, a poly(glycolic acid)/poly(ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone) poly(ethylene glycol) copolymer, a polyorthoester, a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a polyanhydride, a poly(dioxanone), a poly(alkylene alkylate), a copolymer of poly(ethylene glycol) and a polyorthoester, a biodegradable polyurethane, a poly(amino acid), a polyetherester, a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(e-caprolactone) dimethacrylate and n-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and

14

formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. 13, predetermined localized portions 120 of support 122 can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions 120 will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads 126 in support 120 are hollow, then after irradiation and ablation, features 120 will become fenestrations. The fenestrations can be created to make support 122 more porous in nature or to allow release of an active agent from within a support, e.g., from within beads 126. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminescent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the

US 8,287,482 B2

15

support may be allowed to self-position in Schlemm's canal. In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

FIGS. 14A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. 14A, a support 200 can be introduced into the canal using syringe 202 and plunger 204. Syringe 202 has distal end 206 that can be at least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger 204, thereby pushing support 200 into the canal. Referring to FIGS. 14B-C, distal end 208 of guide element 210 can be at least partially introduced into the canal. Guide element 210 can be a guide wire. Guide element 210 can be extended circumferentially along the canal to aid in positioning the support. Support 212 comprises central bore 218 capable of accommodating guide element 210 such that support 212 can be threaded onto guide element 210 and slidably positioned along the guide element. Once distal end 209 of support 212 is threaded onto guide element 210, support 212 can be pushed in a distal direction along guide element 210 to insert support 212 into the canal. In some variations, support 212 can remain threaded onto guide element 210, and guide element 210 can remain in the canal. In other variations, support 212 can be slid off distal end 208 of guide element 210, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. 14C-D, syringe 202 with plunger 204 can be used in combination with a guide element 210. In this variation, distal end 208 of guide element 210 is inserted at least partially into Schlemm's canal. Guide element 210

16

can be extended circumferentially along the canal to aid in positioning the support. Support 212 has central bore 218 capable of accommodating guide element 210. Proximal end 211 of guide element 210 is inserted into bore 218. Plunger 204 is depressed in a distal direction to push support 212 into the canal and slide support 212 along element 210. Guide element 210 can remain in the canal or be removed following insertion of the support. Supports 200, 212 must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more minors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. 11A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

What we claim is:

1. A device comprising:

a support having at least one fenestration that is longitudinally insertable into a lumen of Schlemm's canal, the support having a cross-sectional dimension sufficient to at least partially prop open Schlemm's canal upon insertion into the canal, and to thereby maintain patency of at least a portion of the canal so that fluid may traverse the canal without substantial interference from the support, wherein when the support is disposed within a lumen of Schlemm's canal, contact between the support and a wall of the canal is discontinuous along a perimeter of the lumen of the canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.

2. The device of claim 1, wherein the support makes minimal contact with the interior surface of the canal wall when the support is disposed within the lumen of the canal.

3. The device of claim 1, wherein the support makes only tangential contact with the canal wall when the support is disposed within the lumen of the canal.

4. The device of claim 1, wherein the support makes only point contacts with the wall of the canal when the support is disposed within the lumen of the canal.

5. The device of claim 1, wherein the support comprises fluted edges.

6. The device of claim 5, wherein only outer peripheral edges of the support contact the canal wall when the support is disposed within the lumen of the canal.

7. The device of claim 1, wherein the support comprises elements that make periodic contact with the canal wall when the support is disposed within the lumen of the canal.

8. The device of claim 1, wherein the support comprises a biocompatible metal.

9. The device of claim 1, wherein the support comprises a biocompatible polymer.

10. The device of claim 1, wherein the support comprises a shape memory material.

11. The device of claim 10, wherein the support comprises a nickel titanium alloy.

12. The device of claim 10, wherein the support is compressible into a first configuration and expandable into a second configuration.

13. The device of claim 12, wherein the support is adapted to be thermally activated to be expanded into the second configuration.

14. The device of claim 1, wherein the support comprises a metal wire.

15. The device of claim 1, wherein the support has a unitary structure.

16. The device of claim 15, wherein the support has a sinusoidal or zig-zag configuration.

17. The device of claim 1, wherein the support has an open network structure.

18. The device of claim 1, wherein the support comprises multiple connected elements configured to be distributed lon-

US 8,287,482 B2

19

gitudinally along Schlemm's canal when the device is in use, and wherein at least one of the connected elements has a cross-sectional dimension sufficient to at least partially prop open Schlemm's canal, and to thereby maintain patency of at least a portion of the canal.

19. The device of claim 18, wherein when the support is disposed within the lumen of Schlemm's canal, at least one region of the support that is located between first and second adjacent connected elements does not contact the wall of the canal.

20. The device of claim 18, wherein at least one of the connected elements is ovoid.

21. The device of claim 18, wherein the at least one fenestration is included in at least one of the connected elements.

22. The device of claim 1, wherein the support is configured to be disposed entirely within Schlemm's canal.

23. The device of claim 1, wherein at least a portion of the support is porous.

24. The device of claim 1, wherein the support contacts less than 10% of C.

25. The device of claim 1, wherein the support contacts less than 1% of C.

26. The device of 1, wherein the support comprises an active agent.

27. The device of claim 26, wherein the active agent comprises a prostaglandin.

28. The device of claim 26, wherein the active agent comprises a prostaglandin analog.

29. The device of claim 1, wherein the support occupies at least a portion of a central core of the canal.

30. The device of claim 1, wherein at least a portion of the support has a polyhedral shape.

31. The device of claim 1, wherein the support is non-tubular.

32. A device comprising:

a support having at least one fenestration that is longitudinally insertable into a lumen of Schlemm's canal, the support comprising an exterior surface and having a cross-sectional dimension sufficient to at least partially prop open Schlemm's canal upon insertion into the canal, and to thereby maintain patency of at least a portion of the canal so that fluid may traverse the canal without substantial interference from the support,

wherein when the support is disposed within a lumen of Schlemm's canal, only a portion of the exterior surface of the support contacts an inner periphery of the lumen of the canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.

33. The device of claim 32, wherein the support makes minimal contact with the interior surface of the canal wall when the support is disposed within the lumen of the canal.

34. The device of claim 32, wherein the support makes only tangential contact with a wall of the canal when the support is disposed within the lumen of the canal.

35. The device of claim 32, wherein the support makes only point contacts with a wall of the canal when the support is disposed within the lumen of the canal.

36. The device of claim 32, wherein the support comprises fluted edges.

37. The device of claim 36, wherein only outer peripheral edges of the support contact the wall of the canal when the support is disposed within the lumen of the canal.

38. The device of claim 32, wherein the support comprises elements that make periodic contact with the canal wall when the support is disposed within the lumen of the canal.

20

39. The device of claim 32, wherein the support comprises a biocompatible metal.

40. The device of claim 32, wherein the support comprises a biocompatible polymer.

41. The device of claim 32, wherein the support comprises a shape memory material.

42. The device of claim 41, wherein the support comprises a nickel titanium alloy.

43. The device of claim 41, wherein the support is compressible into a first configuration and expandable into a second configuration.

44. The device of claim 43, wherein the support is adapted to be thermally activated to be expanded into the second configuration.

45. The device of claim 32, wherein the support comprises a metal wire.

46. The device of claim 32, wherein the support has a unitary structure.

47. The device of claim 46, wherein the support has a sinusoidal or zig-zag configuration.

48. The device of claim 32, wherein the support has an open network structure.

49. The device of claim 32, wherein the support comprises multiple connected elements configured to be distributed longitudinally along Schlemm's canal when the device is in use, and wherein at least one of the connected elements has a cross-sectional dimension sufficient to at least partially prop open Schlemm's canal, and to thereby maintain patency of at least a portion of the canal.

50. The device of claim 49, wherein when the support is disposed within the lumen of Schlemm's canal, at least one region of the support that is located between first and second adjacent connected elements does not contact the wall of the canal.

51. The device of claim 49, wherein at least one of the connected elements is ovoid.

52. The device of claim 49, wherein the at least one fenestration is included in at least one of the connected elements.

53. The device of claim 32, wherein the support is configured to be disposed entirely within Schlemm's canal.

54. The device of claim 32, wherein at least a portion of the support is porous.

55. The device of claim 32, wherein the support contacts less than 10% of C.

56. The device of claim 32, wherein the support contacts less than 1% of C.

57. The device of 32, wherein the support comprises an active agent.

58. The device of claim 57, wherein the active agent comprises a prostaglandin.

59. The device of claim 57, wherein the active agent comprises a prostaglandin analog.

60. The device of claim 32, wherein the support occupies at least a portion of a central core of the canal.

61. The device of claim 32, wherein at least a portion of the support has a polyhedral shape.

62. The device of claim 32, wherein the support is non-tubular.

63. A method for reducing intraocular pressure in an eye, the method comprising:

inserting a support having at least one fenestration into a lumen of Schlemm's canal to at least partially prop open the canal and thereby maintain patency of at least a portion of the canal,

wherein when the support is disposed within the lumen of Schlemm's canal, the support allows fluid to traverse the canal without substantial interference from the support,

US 8,287,482 B2

21

and wherein contact between the support and a wall of the canal is discontinuous along a perimeter of the lumen of the canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.

64. The method of claim 63, the method comprising inserting the support into the lumen of Schlemm's canal such that the support is disposed entirely within the canal.

65. The method of claim 63, wherein the support makes minimal surface area contact with the canal wall when the support is disposed within the lumen of the canal.

66. The method of claim 63, wherein the support makes only tangential contact with the wall of the canal when the support is disposed within the lumen of the canal.

67. The method of claim 63, wherein the support makes only point contacts with the wall of the canal with the support is disposed within the lumen of the canal.

68. The method of claim 63, wherein the support comprises fluted edges that contact the wall of the canal.

69. The method of claim 63, wherein the support comprises elements that make periodic contact with the canal wall when the support is disposed within the lumen of the canal.

70. The method of claim 63, wherein the support has a unitary structure.

71. The method of claim 70, wherein the support has a sinusoidal or zig-zag structure.

72. The method of claim 63, wherein the support comprises a metal wire.

73. The method of claim 63, wherein the support comprises multiple connected elements distributed longitudinally along Schlemm's canal when the support is disposed within the lumen of the canal, and wherein at least one of the elements

22

has a cross-sectional dimension sufficient to at least partially prop open the canal to thereby maintain patency of at least a portion of the canal.

74. The method of claim 63, wherein the support contacts less than 10% of C.

75. The method of claim 63, wherein the support contacts less than 1% of C.

76. The method of claim 63, wherein the support has an open network structure.

77. The method of claim 63, wherein the support comprises a biocompatible metal.

78. The method of claim 63, wherein the support comprises a biocompatible polymer.

79. The method of claim 63, wherein the support comprises a shape memory material.

80. The method of claim 79, wherein the shape memory material comprises a nickel titanium alloy.

81. The method of claim 79, wherein the support is compressible into a first configuration and expandable into a second configuration.

82. The method of claim 79, wherein the support is adapted to be thermally activated to be expanded into the second configuration.

83. The method of claim 63, wherein the support delivers an active agent to the eye.

84. The method of claim 83, wherein the active agent comprises a prostaglandin.

85. The method of claim 83, wherein the active agent comprises a prostaglandin analog.

86. The method of claim 63, wherein the support occupies at least a portion of a central core of the canal.

* * * * *

EXHIBIT B



US009370443B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.:** **US 9,370,443 B2**
(45) **Date of Patent:** **Jun. 21, 2016**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

(75) Inventors: **David Y. Badawi**, Northbrook, IL (US);
Paul Badawi, San Francisco, CA (US)

(73) Assignee: **Sight Sciences, Inc.**, Menlo Park, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 868 days.

(21) Appl. No.: **13/025,112**

(22) Filed: **Feb. 10, 2011**

(65) **Prior Publication Data**

US 2011/0130831 A1 Jun. 2, 2011

Related U.S. Application Data

(62) Division of application No. 11/475,523, filed on Jun. 26, 2006, now Pat. No. 7,909,789.

(51) **Int. Cl.**

A61M 5/00 (2006.01)

A61F 9/007 (2006.01)

(52) **U.S. Cl.**

CPC **A61F 9/00781** (2013.01); **A61F 2210/0004** (2013.01); **A61F 2210/0014** (2013.01); **A61F 2250/0067** (2013.01)

(58) **Field of Classification Search**

CPC A61F 9/00781; A61F 2210/0014; A61F 2250/0067

USPC 604/8, 9, 264; 623/23.64, 23.7
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,159,161 A 12/1964 Ness
4,068,664 A 1/1978 Sharp et al.
4,457,757 A 7/1984 Molteno

4,553,545 A 11/1985 Maass et al.
4,719,825 A 1/1988 LaHaye et al.
4,936,825 A 6/1990 Ungerleider
4,957,505 A 9/1990 McDonald
5,180,362 A 1/1993 Worst

(Continued)

FOREIGN PATENT DOCUMENTS

JP 2002-541976 A 12/2002
JP 2003-180730 A 7/2003

(Continued)

OTHER PUBLICATIONS

Boyle, E.L. (Feb. 1, 2006). "New Glaucoma Devices Take Different Approaches to IOP Lowering," *Ocular Surgery News U.S. Edition*, located at <<http://www.osnsupersite.com/view.aspx?rid=12436>>, last visited on Apr. 23, 2012, 4 pages.

(Continued)

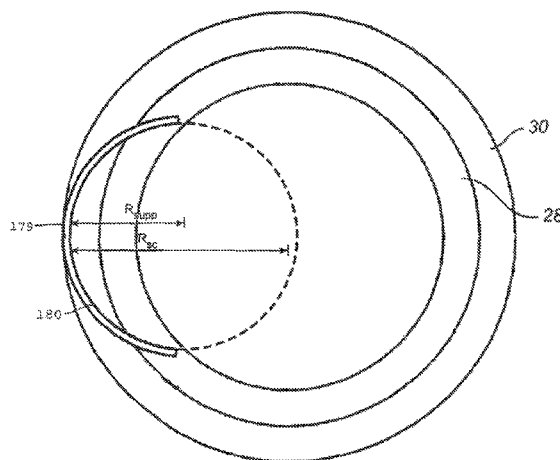
Primary Examiner — Leslie Deak

(74) *Attorney, Agent, or Firm* — Morrison & Foerster LLP

(57) **ABSTRACT**

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmurial fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmurial fluid flow across the canal.

71 Claims, 16 Drawing Sheets



(56)

References Cited

U.S. PATENT DOCUMENTS

5,368,572 A 11/1994 Shirota
 5,486,165 A 1/1996 Stegmann
 5,569,197 A 10/1996 Helmus et al.
 5,626,558 A 5/1997 Suson
 5,639,278 A 6/1997 Dereume et al.
 5,868,697 A 2/1999 Richter et al.
 6,050,970 A 4/2000 Baerveldt
 6,299,603 B1 10/2001 Hecker et al.
 6,309,375 B1 10/2001 Glines et al.
 6,375,642 B1 4/2002 Grieshaber et al.
 6,494,857 B1 12/2002 Neuhann
 6,508,779 B1 1/2003 Suson
 6,616,996 B1 9/2003 Keith et al.
 6,736,791 B1 5/2004 Tu et al.
 6,843,792 B2 1/2005 Nishtala et al.
 6,893,415 B2 5/2005 Madsen et al.
 7,207,980 B2 4/2007 Christian et al.
 7,909,789 B2 3/2011 Badawi et al.
 7,951,155 B2 5/2011 Smedley et al.
 7,967,772 B2 6/2011 McKenzie et al.
 8,075,511 B2 12/2011 Tu et al.
 8,287,482 B2 10/2012 Badawi et al.
 8,439,972 B2 5/2013 Badawi et al.
 8,491,549 B2 7/2013 Conston et al.
 8,529,622 B2 9/2013 Badawi et al.
 8,876,898 B2 11/2014 Badawi et al.
 8,894,603 B2 11/2014 Badawi et al.
 9,095,412 B2 8/2015 Badawi et al.
 2002/0013546 A1 1/2002 Grieshaber et al.
 2002/0013572 A1 1/2002 Berlin
 2002/0133168 A1 9/2002 Smedley et al.
 2002/0143284 A1 10/2002 Tu et al.
 2003/0060447 A1 3/2003 Karakelle et al.
 2003/0060873 A1 3/2003 Gertner et al.
 2004/0044310 A1 3/2004 Suzuki
 2004/0193262 A1 9/2004 Shaddock
 2004/0254520 A1 12/2004 Porteous et al.
 2004/0254521 A1 12/2004 Simon
 2004/0260228 A1 12/2004 Lynch et al.
 2005/0055082 A1 3/2005 Ben Muvhar et al.
 2005/0267555 A1 12/2005 Marnfeldt et al.
 2005/0277864 A1 12/2005 Haffner et al.
 2006/0069340 A1 3/2006 Simon
 2006/0195187 A1 8/2006 Stegmann et al.
 2007/0073275 A1 3/2007 Conston et al.
 2007/0191863 A1 8/2007 De Juan et al.
 2007/0276420 A1 11/2007 Sorensen et al.
 2007/0298068 A1 12/2007 Badawi et al.
 2008/0058760 A1 3/2008 Agerup
 2008/0300574 A1 12/2008 Belson et al.
 2009/0036819 A1 2/2009 Tu et al.
 2009/0043321 A1 2/2009 Conston et al.
 2009/0132040 A1 5/2009 Frion et al.
 2009/0227934 A1 9/2009 Euteneuer et al.
 2010/0087774 A1 4/2010 Haffner et al.
 2010/0173866 A1 7/2010 Hee et al.
 2010/0179652 A1 7/2010 Yamamoto et al.
 2010/0191329 A1 7/2010 Badawi et al.
 2010/0222802 A1 9/2010 Gillespie
 2011/0009874 A1 1/2011 Wardle et al.
 2011/0009958 A1 1/2011 Wardle et al.
 2011/0098809 A1 4/2011 Wardle et al.
 2011/0196487 A1 8/2011 Badawi et al.
 2011/0238009 A1 9/2011 Meron et al.
 2012/0059461 A1 3/2012 Badawi et al.
 2012/0136306 A1 5/2012 Bartha
 2012/0197176 A1 8/2012 Badawi et al.
 2012/0310072 A1 12/2012 Grieshaber
 2013/0041346 A1 2/2013 Alon
 2013/0253402 A1 9/2013 Badawi et al.
 2013/0253438 A1 9/2013 Badawi et al.
 2013/0274655 A1 10/2013 Jennings et al.
 2013/0345808 A1 12/2013 Badawi et al.
 2015/0051699 A1 2/2015 Badawi et al.
 2015/0073328 A1 3/2015 Badawi et al.

FOREIGN PATENT DOCUMENTS

JP 2005-510317 A 4/2005
 JP 2005-538809 A 12/2005
 WO WO-00/64393 A1 11/2000
 WO WO-03/045582 A1 6/2003
 WO WO-2004/026361 A1 4/2004
 WO WO-2005/105197 A2 11/2005
 WO WO-2005/105197 A3 11/2005
 WO WO-2005/107664 A2 11/2005
 WO WO-2005/107664 A3 11/2005
 WO WO-2005/117752 A1 12/2005
 WO WO-2006/066103 A2 6/2006
 WO WO-2006/066103 A3 6/2006
 WO WO-2008/002377 A1 1/2008
 WO WO-2009/042596 A2 4/2009
 WO WO-2009/042596 A3 4/2009
 WO WO-2011/097408 A1 8/2011
 WO WO-2011/106781 A1 9/2011
 WO WO-2013/141898 A1 9/2013

OTHER PUBLICATIONS

Final Office Action mailed on Nov. 1, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 12 pages.
 Final Office Action mailed on Jul. 19, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 6 pages.
 Final Office Action mailed on Feb. 1, 2013, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 6 pages.
 International Search Report mailed on Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, 4 pages.
 International Search Report mailed on Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 2 pages.
 Non-Final Office Action mailed on May 17, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 10 pages.
 Non-Final Office Action mailed on Jan. 26, 2012, for U.S. Appl. No. 12/695,053, filed Jan. 27, 2010, 10 pages.
 Non-Final Office Action mailed on Mar. 15, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 4 pages.
 Non-Final Office Action mailed on May 11, 2012, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 5 pages.
 Non-Final Office Action mailed on Nov. 9, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 5 pages.
 Notice of Allowance mailed on Feb. 2, 2011, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 6 pages.
 Notice of Allowance mailed on Jun. 11, 2012, for U.S. Appl. No. 12/695,053, filed Jan. 27, 2010, 7 pages.
 Notice of Allowance mailed on Apr. 2, 2013, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 6 pages.
 Notice of Allowance mailed on May 10, 2013, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 8 pages.
 Restriction Requirement mailed on Sep. 30, 2009, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 9 pages.
 Restriction Requirement mailed on Feb. 23, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 6 pages.
 Restriction Requirement mailed on Mar. 28, 2012, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 7 pages.
 Written Opinion mailed on Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, 6 pages.
 Written Opinion mailed on Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 5 pages.
 Notice of Allowance mailed on Jul. 7, 2014, for U.S. Appl. No. 14/012,963, filed Aug. 28, 2013, 6 pages.
 Restriction Requirement mailed on Sep. 15, 2014, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 6 pages.
 U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, by Badawi et al. (Copy not attached).
 Final Office Action mailed on Apr. 23, 2015, for U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 8 pages.
 Non-Final Office Action mailed on Feb. 4, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 6 pages.
 European Search Report mailed Apr. 22, 2015, for EP Patent Application No. 11740372.5, filed Feb. 3, 2011, six pages.

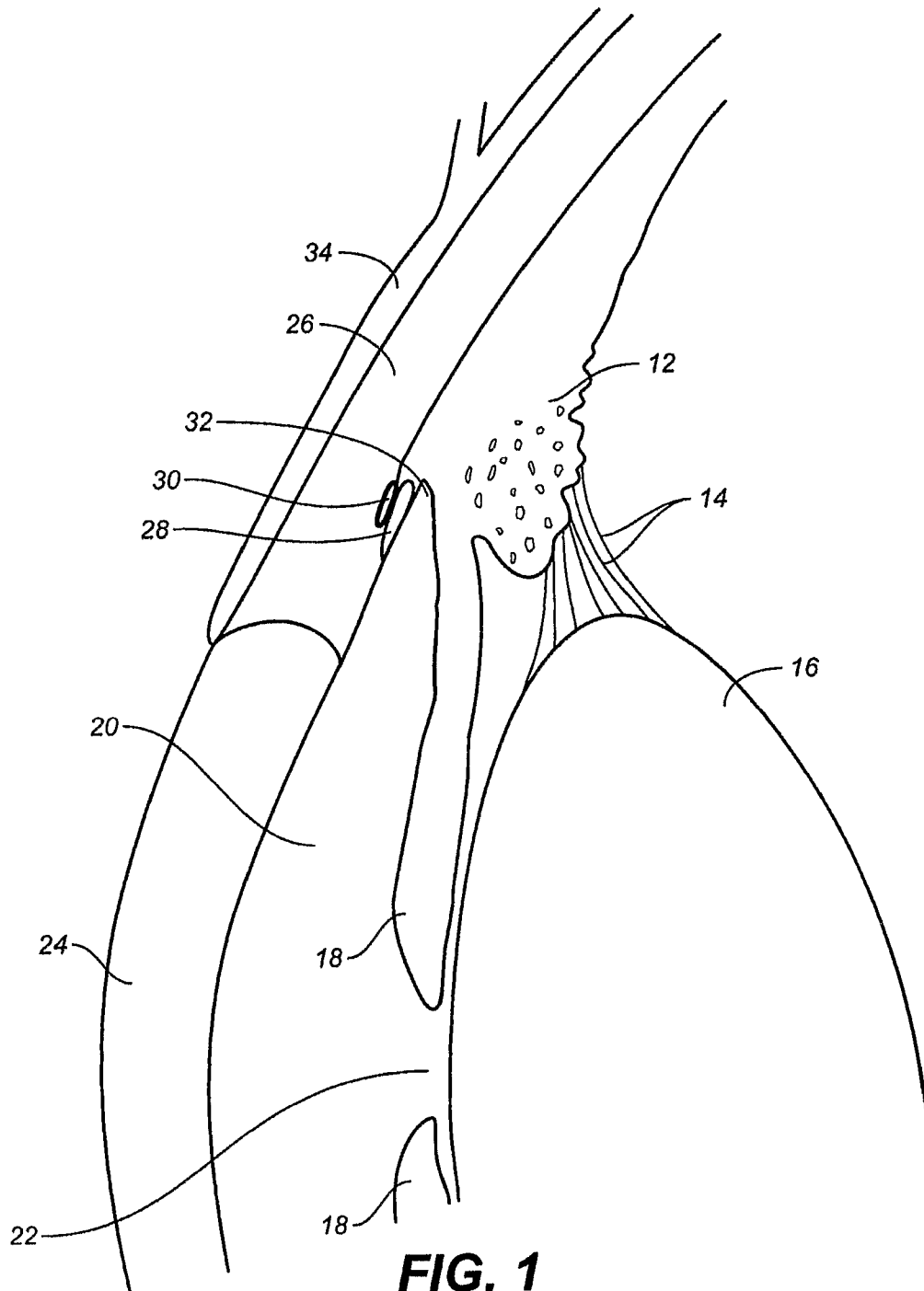
(56)

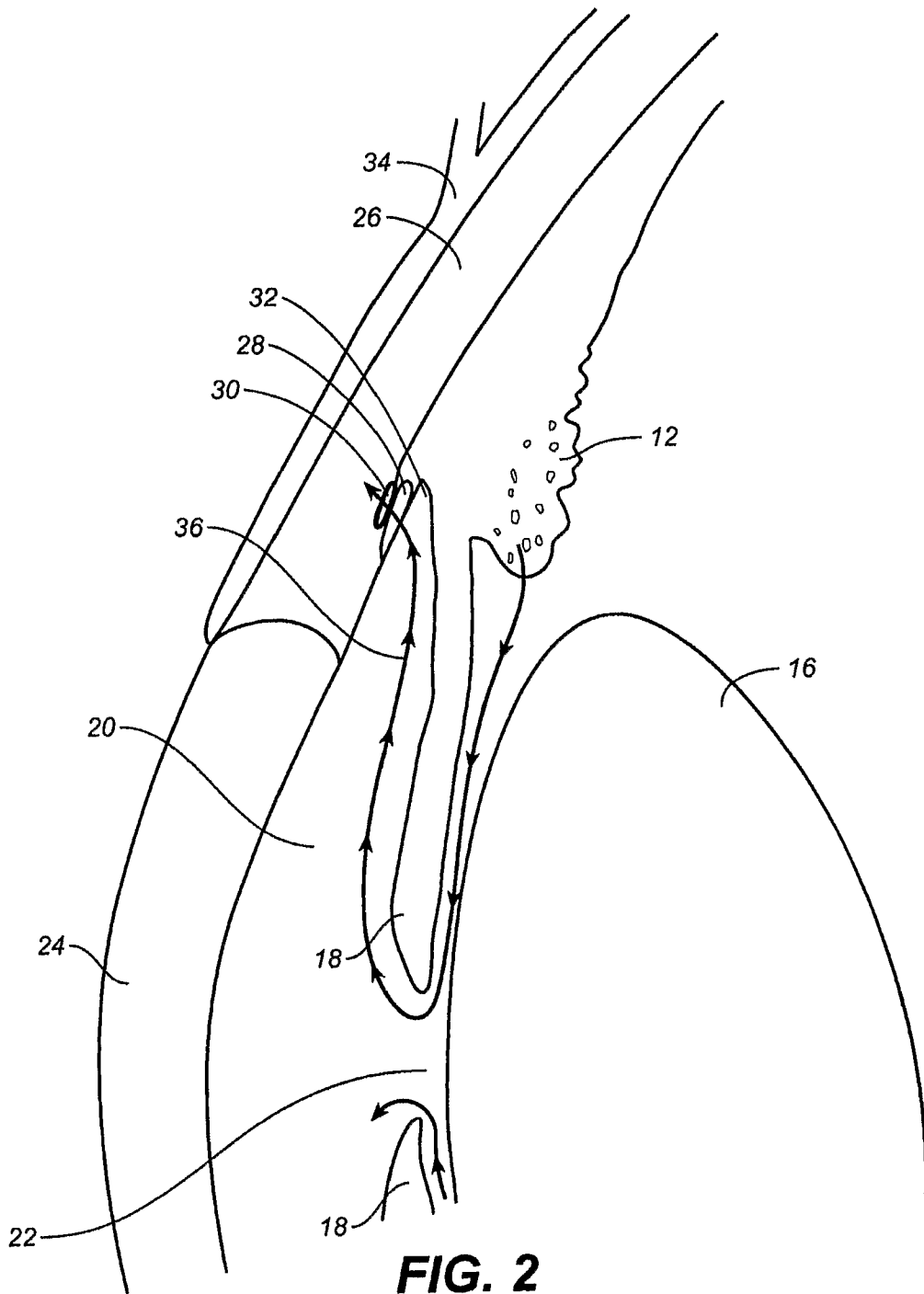
References Cited

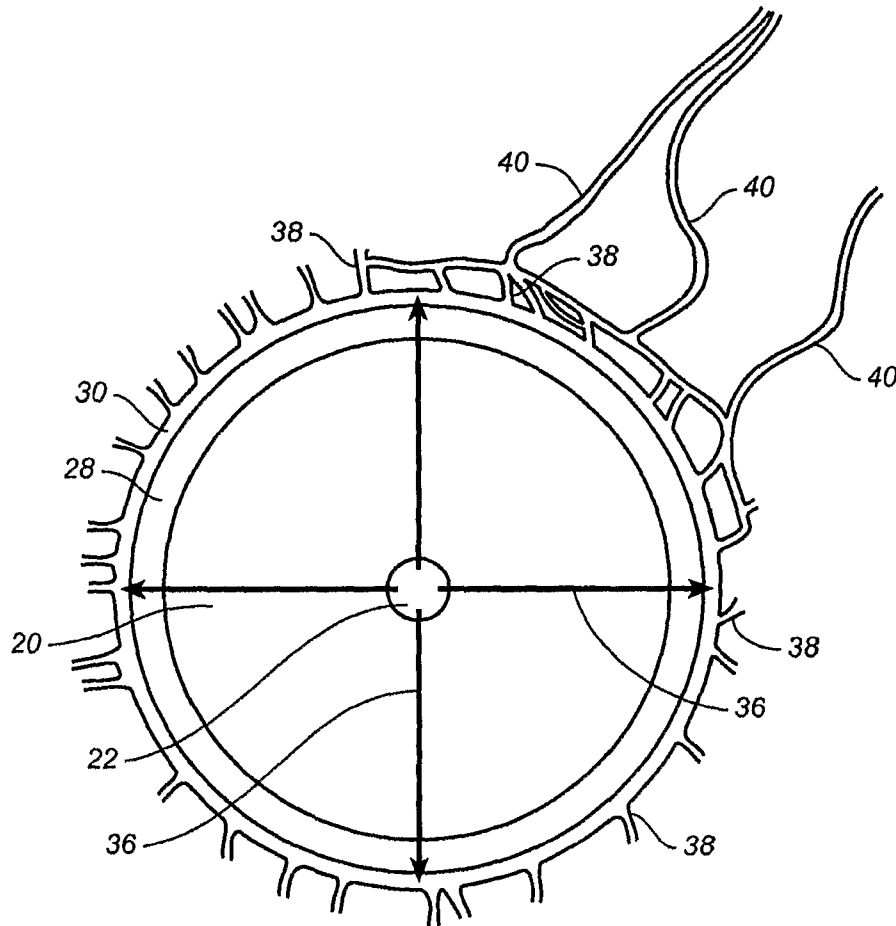
OTHER PUBLICATIONS

Final Office Action mailed on Sep. 20, 2013, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 16 pages.
Final Office Action mailed on Nov. 12, 2013, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 8 pages.
Final Office Action mailed on Jan. 8, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 8 pages.
Final Office Action mailed on Sep. 3, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 8 pages.
Final Office Action mailed on Aug. 19, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 6 pages.
International Search Report mailed on Feb. 1, 2013 for PCT Application No. PCT/US2012/058751, filed on Oct. 4, 2012, 4 pages.
International Search Report mailed on Sep. 14, 2015, for PCT Application No. PCT/US2015/023720, filed on Mar. 31, 2015, 5 pages.
Non-Final Office Action mailed on Apr. 24, 2013, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 13 pages.
Non-Final Office Action mailed on Jun. 12, 2013, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 8 pages.
Non-Final Office Action mailed on Sep. 9, 2013, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.
Non-Final Office Action mailed on Feb. 7, 2014, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 12 pages.
Non-Final Office Action mailed on May 15, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.
Non-Final Office Action mailed on Nov. 28, 2014, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 7 pages.

Non-Final Office Action mailed on Jan. 14, 2015, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 10 pages.
Non-Final Office Action mailed on Oct. 7, 2015, U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 5 pages.
Non-Final Office Action mailed on Nov. 3, 2015, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 7 pages.
Non-Final Office Action mailed on Dec. 14, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 10 pages.
Notice of Allowance mailed on Jul. 23, 2014, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 8 pages.
Notice of Allowance mailed on Mar. 30, 2015, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 5 pages.
Notice of Allowance mailed on Aug. 10, 2015, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.
Restriction Requirement mailed on Sep. 25, 2015, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 6 pages.
Written Opinion mailed on Feb. 1, 2013 for PCT Application No. PCT/US2012/058751, filed Oct. 4, 2012, 6 pages.
Written Opinion mailed on Sep. 14, 2015 for PCT/US2015/023720, filed on Mar. 31, 2015, 8 pages.
U.S. Appl. No. 14/973,620, filed Dec. 17, 2015, by Badawi et al. (Copy not attached).
Final Office Action mailed on Mar. 9, 2016, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 11 pages.
Non-Final Office Action mailed on Feb. 25, 2016, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 19 pages.
Supplementary European Search Report mailed on Mar. 24, 2016, for European Patent Application No. 12871982.0, filed Oct. 4, 2012, 7 pages.





**FIG. 3**

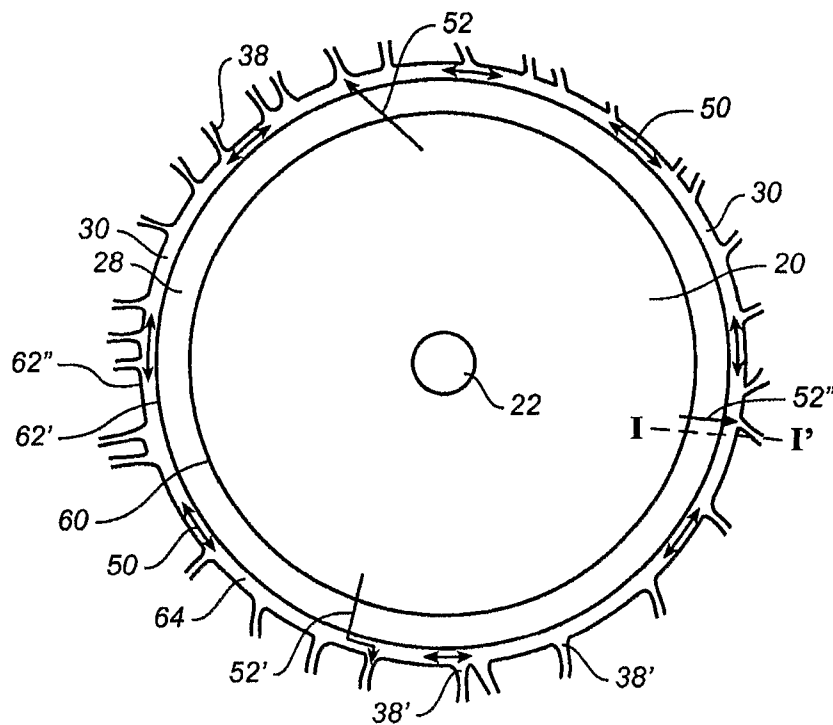


FIG. 4A

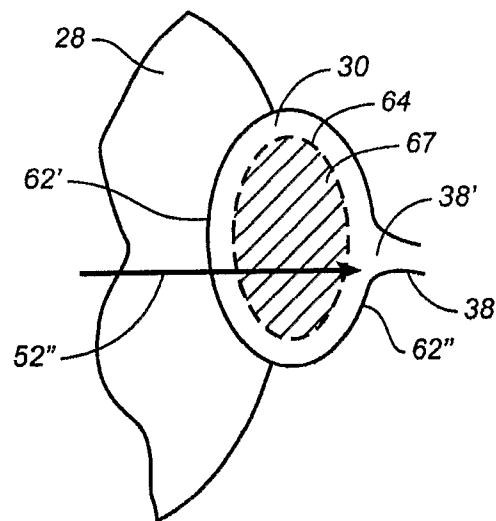


FIG. 4B

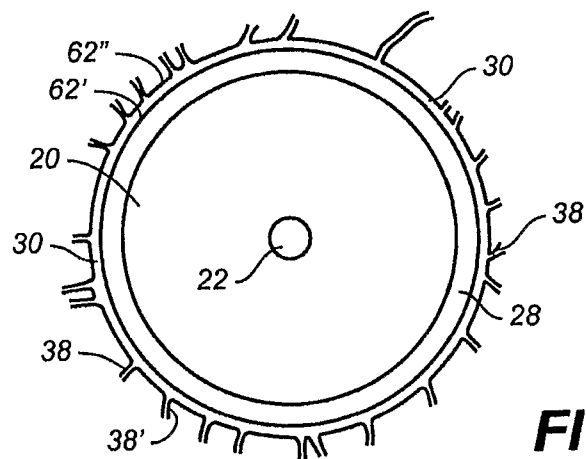


FIG. 5A

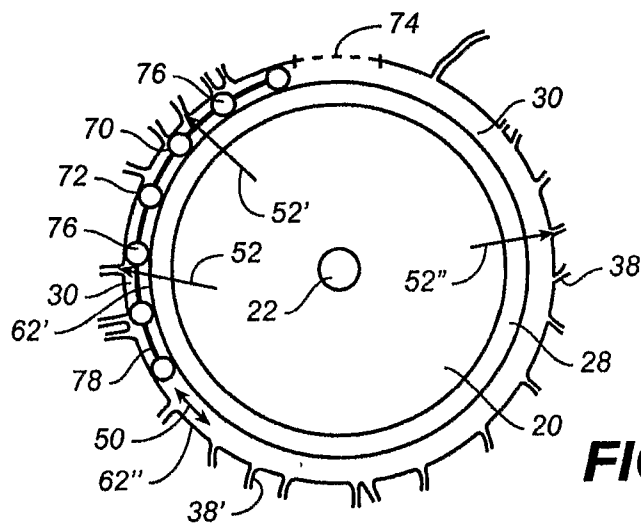


FIG. 5B

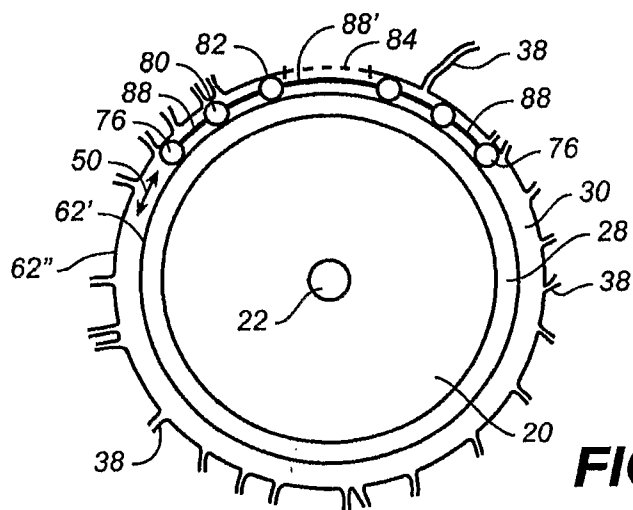


FIG. 5C

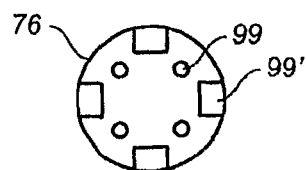
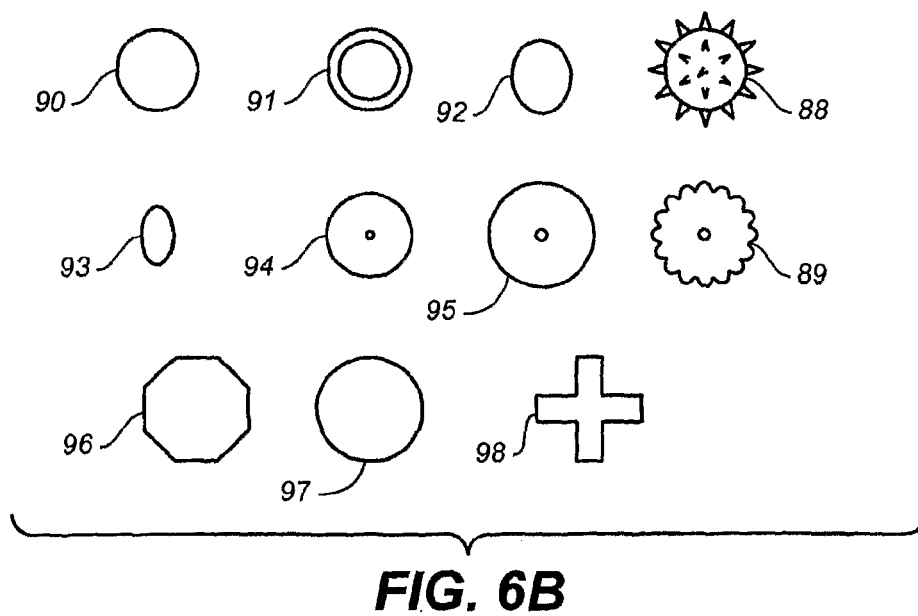
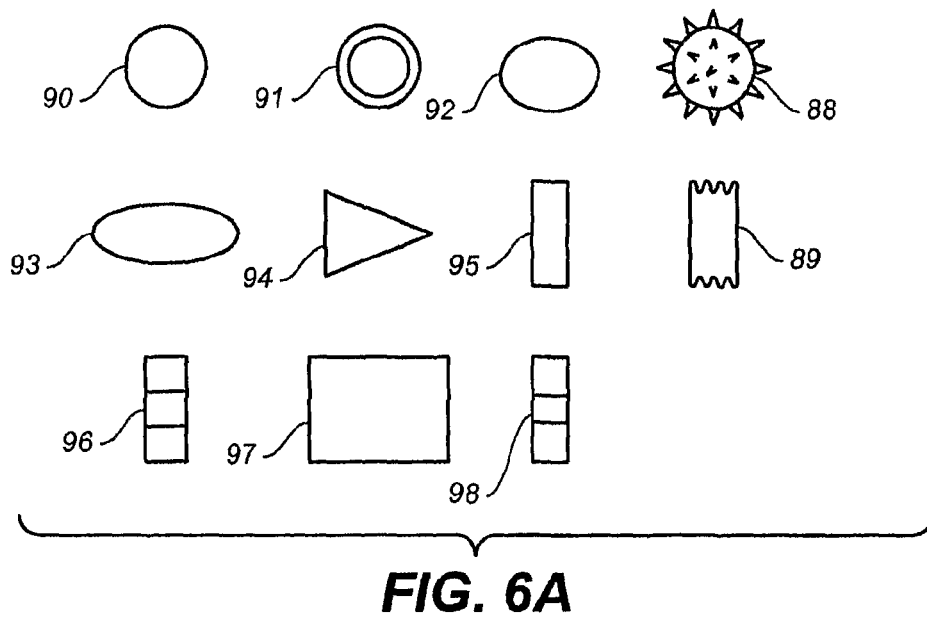


FIG. 6C



FIG. 7A

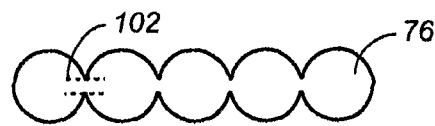


FIG. 7B

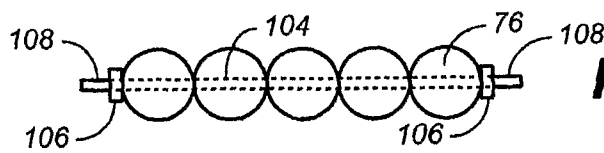


FIG. 7C

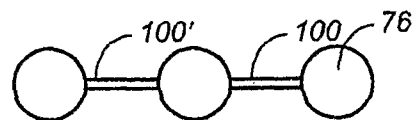


FIG. 7D

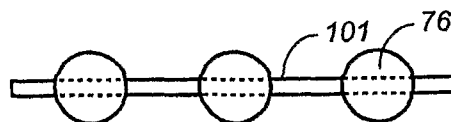


FIG. 7E

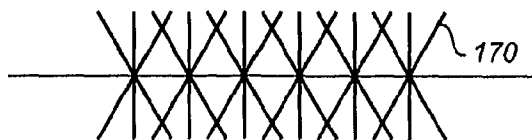


FIG. 8A

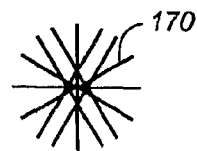


FIG. 8B

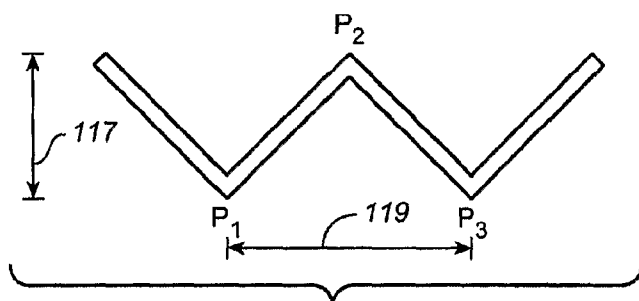


FIG. 8C



FIG. 8D

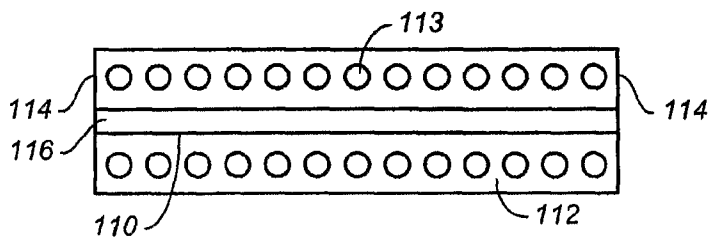


FIG. 8E

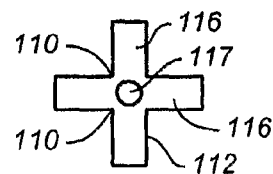


FIG. 8F

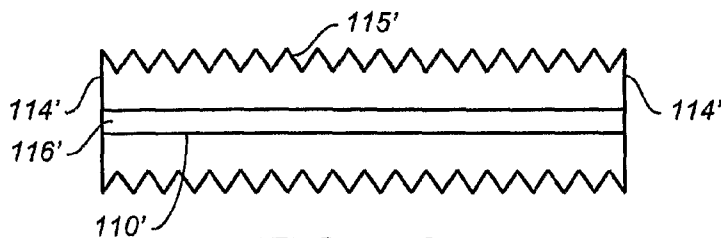


FIG. 8G

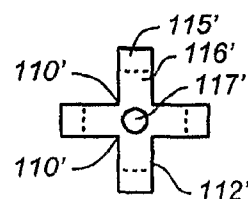


FIG. 8H

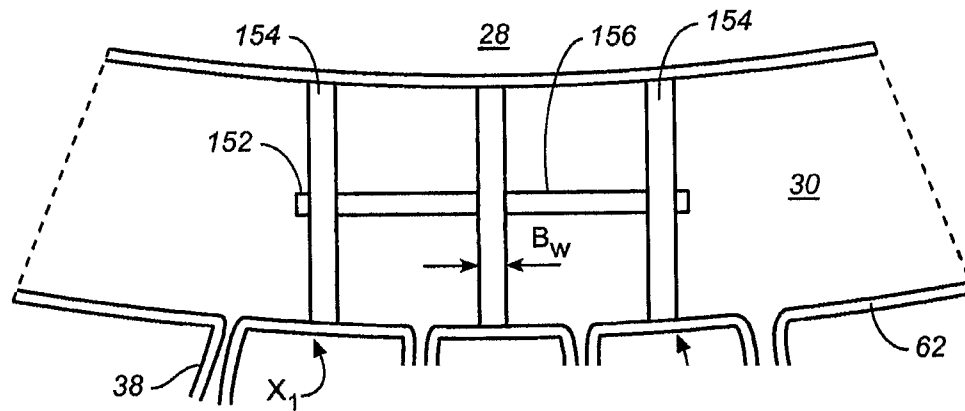


FIG. 9A

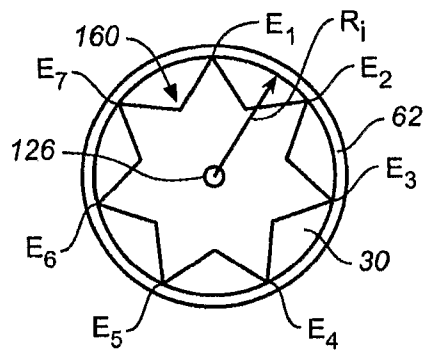


FIG. 9B

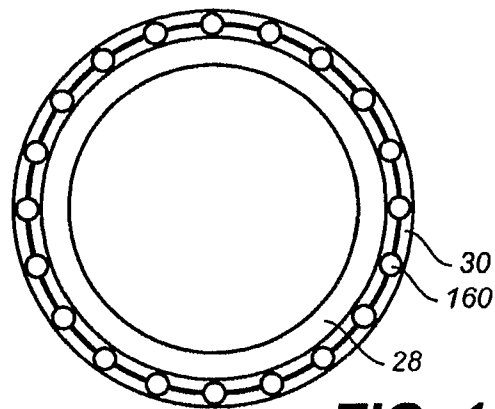


FIG. 10A

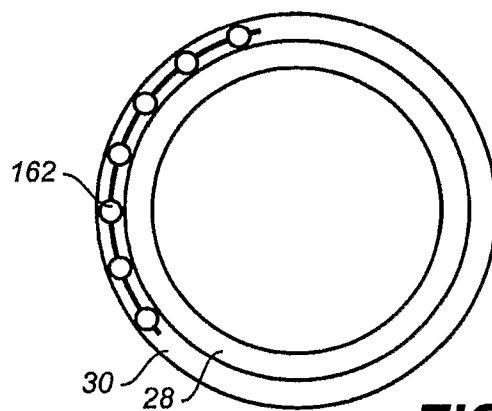


FIG. 10B

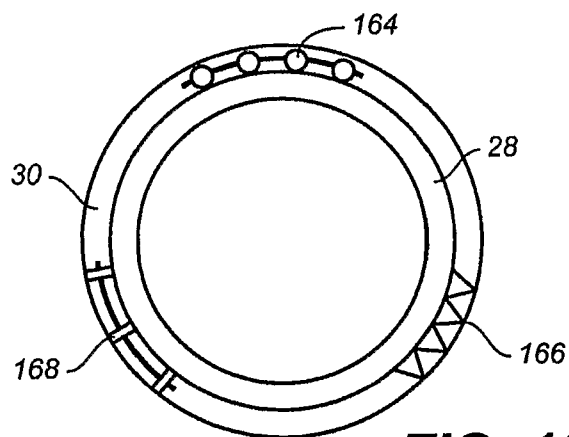
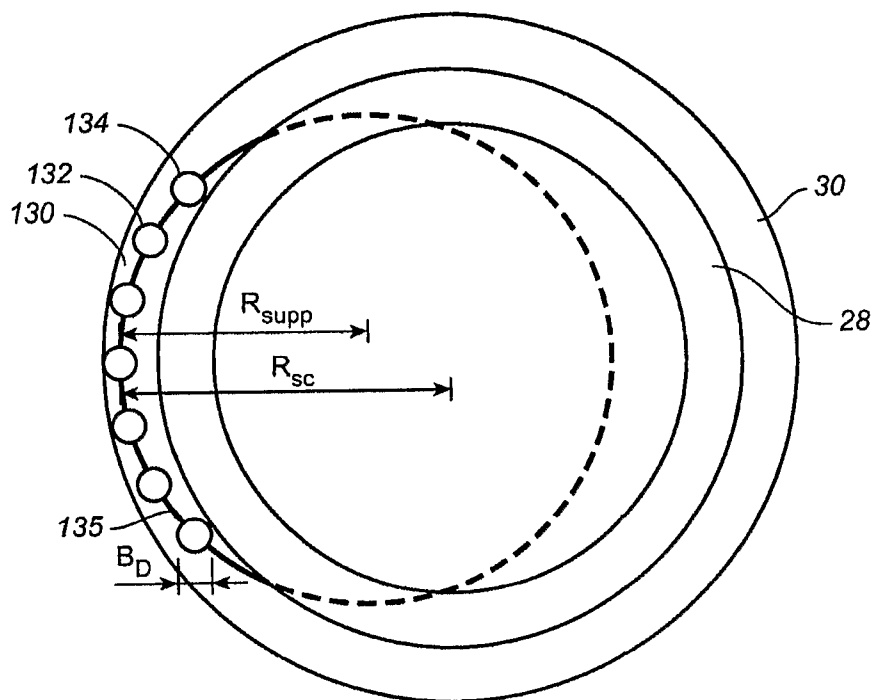


FIG. 10C

**FIG. 11A**

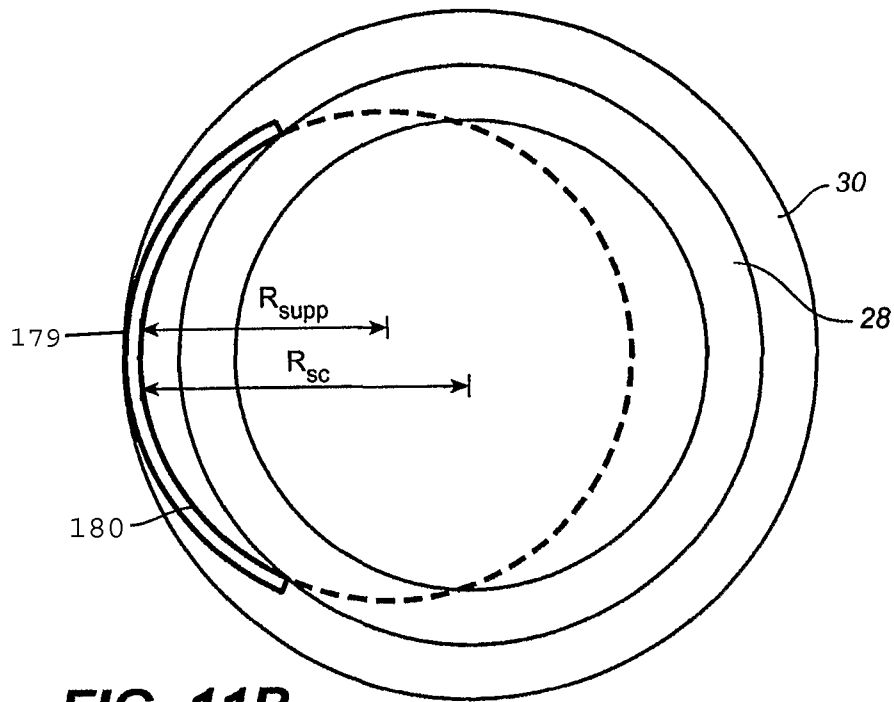


FIG. 11B

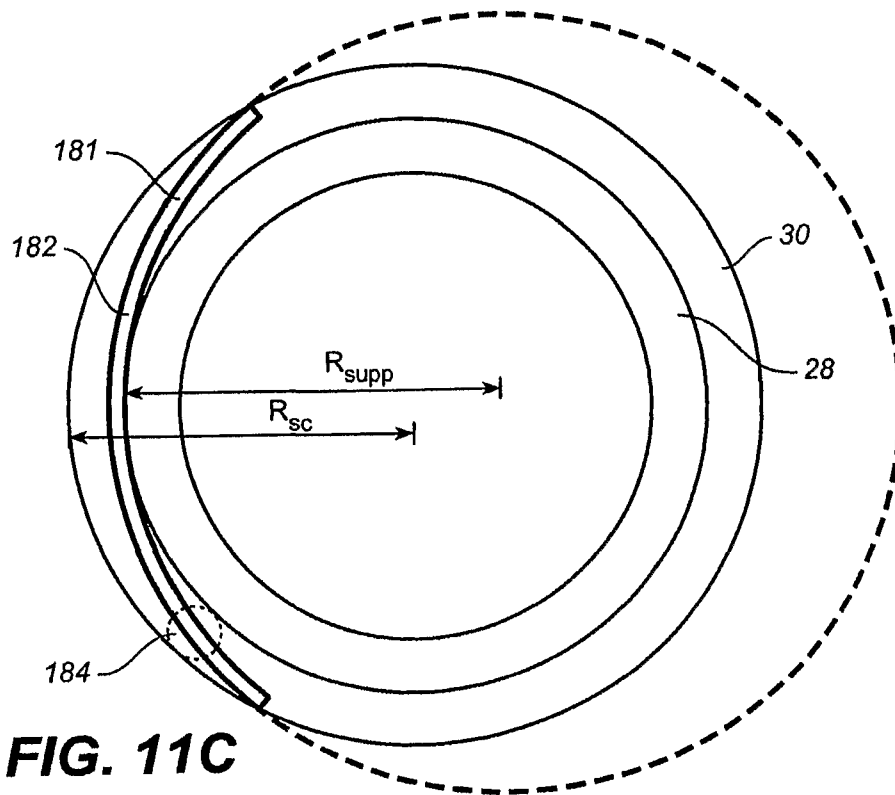
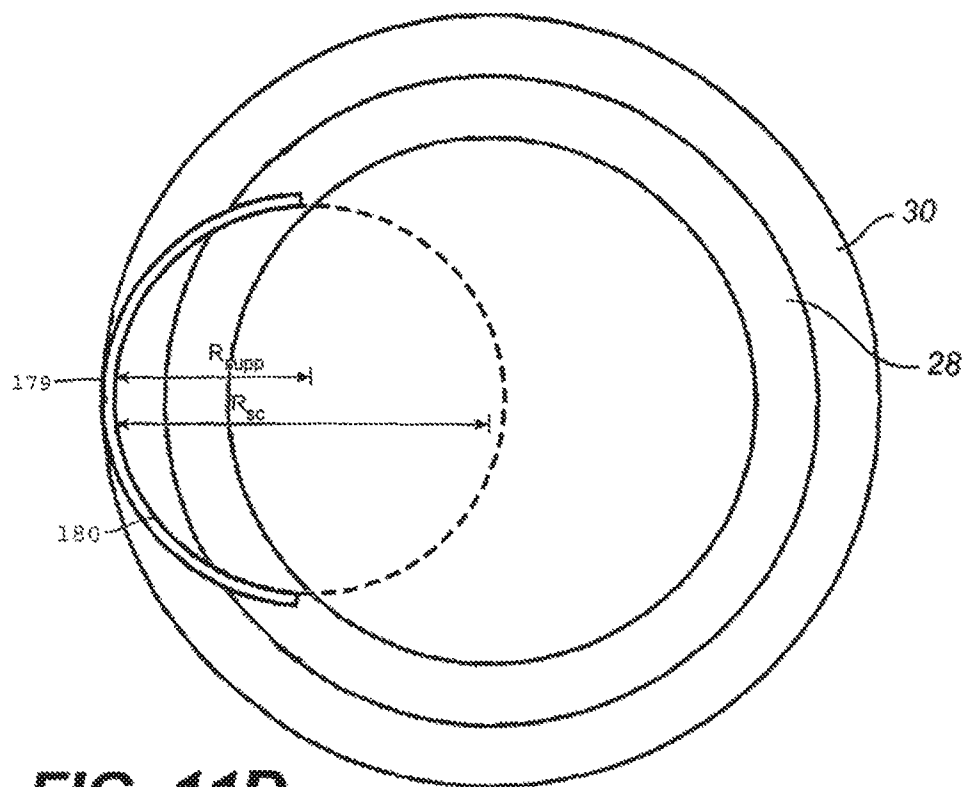


FIG. 11C

**FIG. 11D**

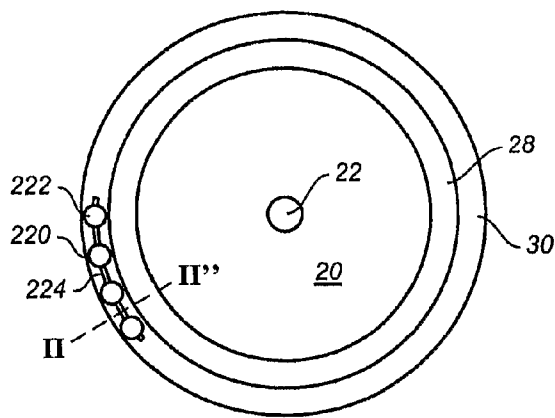


FIG. 12A

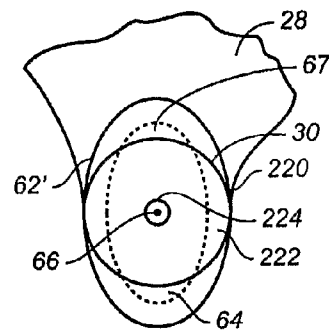


FIG. 12B

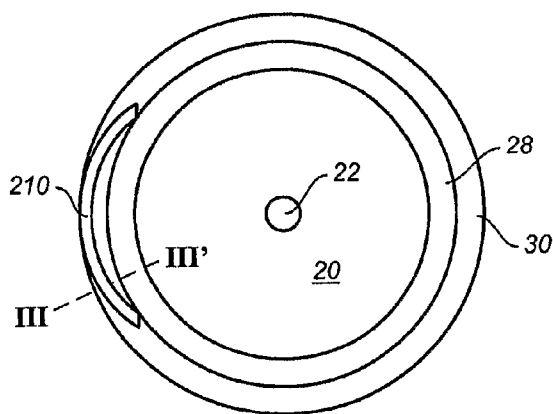


FIG. 12C

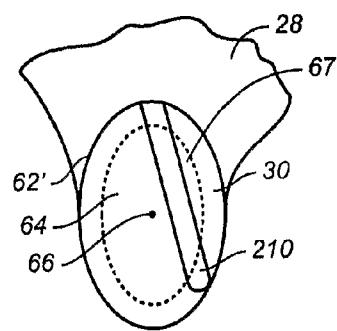


FIG. 12D

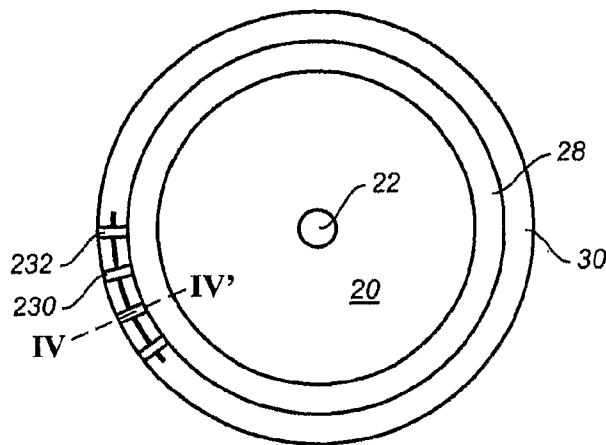


FIG. 12E

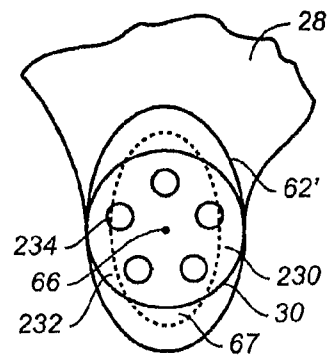


FIG. 12F

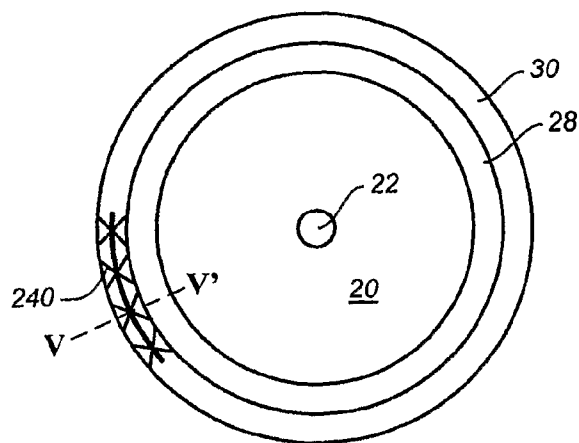


FIG. 12G

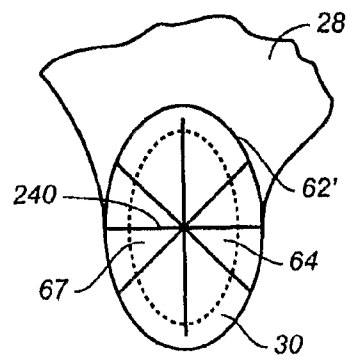


FIG. 12H

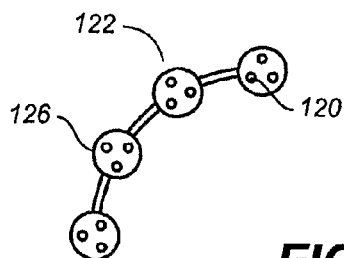


FIG. 13

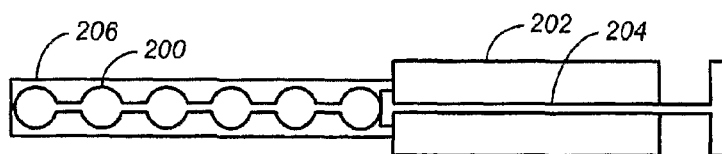


FIG. 14A

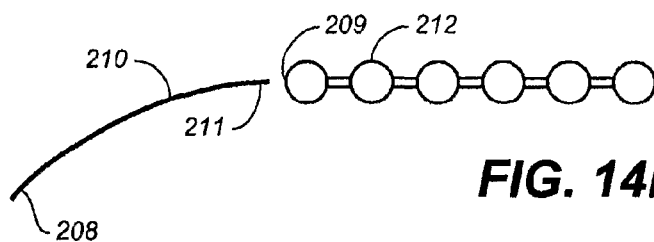


FIG. 14B



FIG. 14C

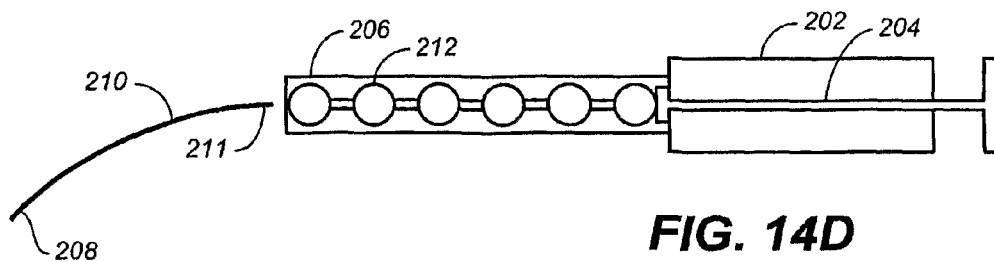


FIG. 14D

1

INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a divisional of U.S. patent application Ser. No. 11/475,523, filed Jun. 26, 2006, the disclosure of which is incorporated herein by reference in its entirety.

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical

2

systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjunctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmural flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal. The support does not substantially interfere with transmural flow across Schlemm's canal, and thereby utilizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocompatible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer; a polyorthoester; a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a poly(anhydride); a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyether-ester; a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, cubical, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted between three beads, the connectors may be of the same or different lengths. The connectors can include the same or different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include

fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmur flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmur flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can include implanting at least two supports. If more than one support is implanted within a single eye, the multiple supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In

5

other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 provides a partial cross-sectional side view of a normal human eye.

FIG. 2 provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. 3 shows a front view of normal fluid drainage from the eye.

FIG. 4A shows an alternative front view of normal fluid drainage paths from the eye. FIG. 4B shows a cross-sectional view along line I-I'.

FIG. 5A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. 5B shows a front view of a device including a support inserted into Schlemm's canal that allows transmurial flow across the canal. FIG. 5C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmurial flow across the canal.

FIG. 6A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. 6B shows the corresponding front views of the element or bead configurations shown in FIG. 6A. FIG. 6C illustrates an element or bead having fenestrations.

FIG. 7A illustrates a support having multiple juxtaposed beads. FIG. 7B illustrates a support having multiple juxtaposed and connected beads. FIG. 7C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. 7D shows a support having multiple, spaced-apart but connected beads. FIG. 7E illustrates beads threaded onto a connector.

FIGS. 8A-B show side and front views, respectively, of a support having an open network structure. FIGS. 8C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at at least three points (labeled P₁, P₂, P₃). FIGS. 8E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. 8G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. 9A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. 10A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. 11A-B and D illustrate configurations of supports having a smaller radius of curvature than Schlemm's canal. FIG. 11C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. 12A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. 12B shows a cross-sectional view along line FIG. 12C illustrates a variation of a support traversing the central core of the canal. FIG. 12D shows a cross-sectional view along line FIG. 12E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. 12F shows a cross-sectional view along line IV-IV'. FIG. 12G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. 12H shows a cross-sectional view along line V-V'.

6

FIG. 13 shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. 14A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. 14B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. 14C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. 14D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmurial fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. 1 shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body 12 is connected to iris 18 and to lens 16 via zonular fibrils 14. The anterior chamber of the eye 20 is bounded on its anterior (front) surface by cornea 24. In the center of iris 18 is pupil 22. Cornea 24 is connected on its periphery to sclera 26, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork 28 is located on the outer peripheral surface of anterior chamber 20. The trabecular meshwork extends 360° circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork 28 is Schlemm's canal 30. Schlemm's canal extends 360° circumferentially around the trabecular meshwork. At the apex formed between iris 18, meshwork 28 and sclera 26 is angle 32. Conjunctiva 34 is a membrane overlaying sclera 26 and lining the inside of the eyelid (not shown).

FIG. 2 shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body 12 and its path through and out of the eye is indicated by solid directional line 36. The aqueous humor flows from ciliary body 12, between lens 16 and iris 18, through pupil 22 into anterior chamber 20, across trabecular meshwork 28, across Schlemm's canal 30, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. 3 shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber 20 via pupil 22. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines 36. The fluid crosses trabecular meshwork 28 and traverses Schlemm's canal 30 to reach aqueous veins or collector channels 38. There are typically 25-30 collector channels located in a human eye. Collector channels 38 are connected to vasculature 40, whereby the drained aqueous humor enters the bloodstream. Although the direction of net or bulk fluid flow is depicted as radially outward by directional lines 36 from pupil 22 for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. 4A-B. FIG. 4A shows a front view of an eye, and FIG. 4B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal 30 is depicted by directional lines 50. Fluid that does not traverse canal 30 to reach collector

7

channels **38** may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines **52**, **52'**, and **52''**. In each of these paths, fluid enters trabecular meshwork **28** along its inner peripheral surface **60** and exits the meshwork along its outer peripheral surface **62'**. Meshwork outer peripheral surface **62'** provides the inner peripheral surface or wall of Schlemm's canal **30**. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork **38** through inner peripheral surface or wall **62'** of Schlemm's canal **30** to reach lumen **64** of the canal. Second, fluid must flow from lumen **64** through canal outer peripheral wall **62''** through apertures **38'** to enter collector channels **38**. Finally, the collector channels **38** feed the drained fluid into vasculature. Lumen **64** of canal **30** includes a central core region **67**. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflow from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1) fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral boundary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the connector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's

8

canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. 5A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal **30**, where canal outer peripheral wall **62''** is very close to canal inner peripheral wall **62'**. Although Schlemm's canal **30** is depicted in FIG. 5A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels **38** is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. 5B illustrates an example of a device **70** inserted into Schlemm's canal **30** through incision site **74**. Device **70** in this example is positioned to one side of incision site **74**. Device **70** includes support **72** that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall **62'** and canal outer wall **62''** to reach collector channels **38** via apertures **38'**. In the example shown in FIG. 5B, support **72** includes elements or beads **76** connected with connectors **78**. In this variation, the distance between canal inner wall **62'** and outer wall **62''** is approximately determined by the cross-sectional dimension of support **72**, which is in turn determined by the largest cross-sectional diameter of the beads **76**. Therefore, circumferential (i.e., longitudinal) fluid flow around and along the canal **30** indicated by directional line **50** may be inhibited by the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52''** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters

(e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. 5C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. 5B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. 6A and 6B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges, **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. 6C, elements or beads **76** may include fenestrations **99**, **99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. 6C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. 7A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. 7A), connected and juxtaposed (FIGS. 7B and 7C), or connected together with connectors **100**, **100'** to form intervals between beads (FIG. 7D). In addition, beads may be threaded onto a connector **101** (FIG. 7E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. 7B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. 7C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knotting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of

external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. 7D, multiple connectors **100**, **100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100**, **100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100**, **100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. 7E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100**, **100'**, **101** can be flexible, such as thin polymer threads or metal wires. Connectors **100**, **100'**, **101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100**, **100'**, **101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. 8A-F. As illustrated in FIG. 8A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. 8A-B will have minimal surface area contact with the walls of Schlemm's canal, i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. 8C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. 8C, the support will contact the wall of Schlemm's canal at at least three points, labeled P_1 , P_2 , and P_3 , after implantation. In FIGS. 8E-H, examples of rod-like supports having fluted edges are shown. In FIGS. 8E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include fenestrations **113**. The support can include central bore **117**. In FIGS. 8G-H, fluted edges **110'** extend along sides **112'** to form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. 8E-H, the support may contact the canal walls at at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. 8A-B shows, some supports only

11

have point contacts with the canal wall. For the supports shown in FIGS. 5B-C, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. 6A-B may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. 7D-E that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. 8C-D, in some variations, the support contacts the interior wall of the canal at at least two points; or at at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided in FIGS. 9A-B. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder C having length L, extending circumferentially from a first end X_1 to a second end X_2 of support **152**, and inside radius R_i . In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder C as described above. In other variations, the support contacts less than 10% of the surface area of C. In still other variations, the support contacts less than 30% of the surface area of C. For example, the support **152** shown in FIGS. 9A-B contacts the canal wall **62** only at bead outer peripheral edges at E_1 - E_7 , along a distance of the bead width B_{bead} . There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmural flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapable metal having a sinusoidal or zig-zag configuration as shown in FIGS. 8C-D, a cross-sectional dimension **117** of the support can be decreased or increased by applying tension along dimension **119**. As illustrated in FIG. 10A, a support **160** can extend essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately half way around the circumference of the canal (not shown). As shown in FIG. 10B, a support **162** can extend less than half way around the canal. As shown in FIG. 10C, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. 11A, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension B_D . Support **132** comprises a stiff arcuate element **135** with a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal R_{SC} . The

12

smaller, fixed radius of curvature R_{supp} of arcuate member **135** urges canal **30** to open more than B_D . In other variations shown in FIGS. 11B and 11D, support **179** comprises an arcuate member **180** without beads having a radius of curvature R_{supp} that is less than the radius of curvature R_{SC} of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. 11C, support **181** comprises an arcuate member **182** having a radius of curvature R_{supp} larger than that of Schlemm's canal R_{SC} . Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. 11C, support **181** can include beads **184**. To urge open the canal, the radius of curvature R_{supp} of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal R_{SC} . For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member R_{supp} in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature R_{supp} of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at at least one point. Referring to FIG. 12A, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. 12B shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. 12C, a front view of an arcuate support **210** is shown. FIG. 12D shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. 12E, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. 12F. As illustrated in FIG. 12F, bead **232** with fenestrations **234** occupies the majority of central core **67** of canal **30**. In other variations, the support occupies only a small portion of the central core of the canal. For example, in FIG. 12G, a front view of a support **240** having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. 12H.

A support can be made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacrylate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives,

13

flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly(lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly(ethylene glycol) copolymer, a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer, a poly(lactic acid)/poly(ethylene glycol) copolymer, a poly(glycolic acid)/poly(ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone)/poly(ethylene glycol) copolymer, a poly(orthoester), a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a poly(anhydride), a poly(dioxanone), a poly(alkylene alkylate), a copolymer of poly(ethylene glycol) and a poly(orthoester), a biodegradable polyurethane, a poly(amino acid), a poly(etherester), a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(ϵ -caprolactone) dimethacrylate and *n*-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and

14

formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. 13, predetermined localized portions 120 of support 122 can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions 120 will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads 126 in support 120 are hollow, then after irradiation and ablation, features 120 will become fenestrations. The fenestrations can be created to make support 122 more porous in nature or to allow release of an active agent from within a support, e.g., from within beads 126. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminescent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the support may be allowed to self-position in Schlemm's canal.

15

In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

FIGS. 14A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. 14A, a support 200 can be introduced into the canal using syringe 202 and plunger 204. Syringe 202 has distal end 206 that can be at least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger 204, thereby pushing support 200 into the canal. Referring to FIGS. 14B-C, distal end 208 of guide element 210 can be at least partially introduced into the canal. Guide element 210 can be a guide wire. Guide element 210 can be extended circumferentially along the canal to aid in positioning the support. Support 212 comprises central bore 218 capable of accommodating guide element 210 such that support 212 can be threaded onto guide element 210 and slidably positioned along the guide element. Once distal end 209 of support 212 is threaded onto guide element 210, support 212 can be pushed in a distal direction along guide element 210 to insert support 212 into the canal. In some variations, support 212 can remain threaded onto guide element 210, and guide element 210 can remain in the canal. In other variations, support 212 can be slid off distal end 208 of guide element 210, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. 14C-D, syringe 202 with plunger 204 can be used in combination with a guide element 210. In this variation, distal end 208 of guide element 210 is inserted at least partially into Schlemm's canal. Guide element 210

16

can be extended circumferentially along the canal to aid in positioning the support. Support 212 has central bore 218 capable of accommodating guide element 210. Proximal end 211 of guide element 210 is inserted into bore 218. Plunger 204 is depressed in a distal direction to push support 212 into the canal and slide support 212 along element 210. Guide element 210 can remain in the canal or be removed following insertion of the support. Supports 200, 212 must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more mirrors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmur flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. 11A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

What we claim is:

1. A device for reducing intraocular pressure in an eye having a Schlemm's canal and a trabecular meshwork, comprising: a support implantable circumferentially within Schlemm's canal and configured to maintain the patency of at least a portion thereof, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than the radius of curvature of Schlemm's canal so that at least a portion of the arcuate member is configured to extend out of Schlemm's canal and into the trabecular meshwork and wherein the support does not substantially interfere with transmur flow across Schlemm's canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.

2. The device of claim 1 wherein the support comprises an active agent.

3. The device of claim 2 wherein the support is coated or impregnated with the active agent.

4. The device of claim 2 wherein the active agent is dispersed within the support.

5. The device of claim 2 wherein the active agent is selected from the group consisting of prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, anti-metabolites, chemotherapeutic agents, steroids, antagonists of growth factors, and combinations thereof.

6. The device of claim 2 wherein the active agent is capable of release using electromagnetic radiation.

7. The device of claim 2 wherein release of the active agent is controllable using a time release system.

8. The device of claim 1 wherein the support has at least one fenestration.

9. The device of claim 1 wherein the shape of the support is capable of alteration using electromagnetic radiation.

10. The device of claim 9 wherein the electromagnetic radiation comprises a laser having a wavelength absorbable by at least one localized portion of the support.

11. The device of claim 1 wherein the support has a circumference equal to about half or less than half of the circumference of Schlemm's canal.

12. The device of claim 1 wherein the support has a circumference equal to about a quarter or less than a quarter of the circumference of Schlemm's canal.

13. The device of claim 1 wherein at least a portion of the support is made from a biocompatible polymer.

14. The device of claim 13 wherein the biocompatible polymer is selected from the group consisting of acrylics and silicones.

15. The device of claim 13 wherein the biocompatible polymer comprises a biodegradable polymer.

16. The device of claim 15 wherein the biodegradable polymer is selected from the group consisting of collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/

19

poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); poly(caprolactone)/poly(ethylene glycol) copolymer; a poly(orthoester); a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a polyanhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

17. The device of claim 13 wherein at least a portion of the support is made from polymethylmethacrylate.

18. The device of claim 1 wherein the support is capable of visual enhancement using fluorescence or phosphorescence emission.

19. The device of claim 18 wherein the support comprises a chromophore that fluoresces or phosphoresces upon excitation with a light source.

20. The device of claim 18 wherein the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm.

21. The device of claim 1 wherein at least a portion of the support is made from a shape memory material.

22. The device of claim 21 wherein the shape memory material comprises a shape memory polymer.

23. The device of claim 21 wherein the shape memory material comprises a shape memory alloy.

24. The device of claim 23 wherein the shape memory alloy comprises a nickel titanium alloy.

25. The device of claim 21 wherein the support has a compressed state prior to and during implantation and an expanded state following implantation.

26. The device of claim 1 wherein at least a portion of the support is made from a hydrogel.

27. The device of claim 1 wherein at least a portion of the support is made from a biocompatible metal.

28. The device of claim 27 wherein the metal is gold.

29. The device of claim 1 wherein the support comprises at least two adjacent beads.

30. The device of claim 29 wherein the at least two adjacent beads are of different sizes.

31. The device of claim 29 wherein the at least two adjacent beads are of different shapes.

32. The device of claim 29 wherein the shapes of the at least two adjacent beads are independently selected from the group consisting of a sphere, a spheroid, an ovoid, a cylinder, a cuboid, a cube, a cone, a discoid, a coil, and combinations and segments thereof.

33. The device of claim 29 further comprising a connector linking the at least two adjacent beads.

34. The device of claim 33 wherein the connector is flexible.

35. The device of claim 33 further comprising at least three adjacent beads, wherein each bead is linked to its adjacent bead by a connector.

36. The device of claim 35 wherein each connector has a different length.

37. The device of claim 33 wherein the connector comprises the same material as the beads.

38. The device of claim 33 wherein the connector comprises a different material than the beads.

20

39. The device of claim 33 wherein the connector is also a spacer configured to provide a space between adjacent beads.

40. The device of claim 1 wherein the support comprises at least two discs separated by, and connected with, a connector.

41. The device of claim 40 wherein at least one of the discs has at least one fenestration.

42. The device of claim 1 wherein the support is configured to contact a wall of Schlemm's canal at least at two points.

43. The device of claim 42 wherein the support is configured to contact a wall of Schlemm's canal at least at three points.

44. The device of claim 1 wherein the support is solid.

45. The device of claim 1 wherein at least a portion of the support is hollow.

46. The device of claim 1 wherein at least a portion of the support is porous.

47. The device of claim 1 wherein at least a portion of the support is made of a mesh.

48. The device of claim 1 wherein the support comprises one or more rod-like members.

49. The device of claim 1 wherein the support is capable of being attached to tissue.

50. The device of claim 1 wherein the support contacts less than 10% of C.

51. The device of claim 1 wherein the support contacts less than 1% of C.

52. The device of claim 1 wherein the support is flexible.

53. The device of claim 1 wherein the support is rigid.

54. The device of claim 1 wherein the support has a cross-sectional diameter of about 50 microns to about 500 microns.

55. The device of claim 1 wherein the support has a cross-sectional diameter of about 190 microns to about 370 microns.

56. The device of claim 1 wherein the support does not substantially interfere with longitudinal flow along Schlemm's canal.

57. The device of claim 1 wherein the support does not substantially interfere with transmur flow into and out of Schlemm's canal.

58. A kit for reducing intraocular pressure in an eye having a Schlemm's canal and a trabecular meshwork comprising:

a support implantable circumferentially within Schlemm's canal and configured to maintain the patency of at least a portion thereof, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than the radius of curvature of curvature of Schlemm's canal so that at least a portion of the arcuate member is configured to extend out of Schlemm's canal and into the trabecular meshwork and wherein the support does not substantially interfere with transmur flow across Schlemm's canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C; and

an introducer for delivering the support.

59. The kit of claim 58 further comprising instructions on using the kit.

60. The kit of claim 58 further comprising an active agent.

61. The kit of claim 58 comprising at least two supports.

62. The kit of claim 61 comprising at least two introducers for delivering the at least two supports.

63. The kit of claim 61 wherein the at least two supports are of different shapes.

64. The kit of claim 61 wherein the at least two supports are of different sizes.

65. The kit of claim 61 wherein the at least two supports comprise different materials.

66. The kit of claim 61 wherein the at least two supports are connected together.

67. The kit of claim 58 further comprising a fixation device 5
for attaching the support to tissue.

68. The kit of claim 58 further comprising a system for visually enhancing the support.

69. The kit of claim 58 further comprising a positioning device for positioning the support. 10

70. The kit of claim 58 wherein the support is preloaded into the introducer.

71. The kit of claim 58 wherein the introducer comprises a pusher.

* * * * *

EXHIBIT C



US009486361B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.:** **US 9,486,361 B2**
(45) **Date of Patent:** **Nov. 8, 2016**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

(75) Inventors: **David Y. Badawi**, Glenview, IL (US);
Paul Badawi, San Francisco, CA (US)

(73) Assignee: **Sight Sciences, Inc.**, Menlo Park, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 577 days.

(21) Appl. No.: **13/445,816**

(22) Filed: **Apr. 12, 2012**

(65) **Prior Publication Data**

US 2012/0197176 A1 Aug. 2, 2012

Related U.S. Application Data

(63) Continuation of application No. 12/695,053, filed on Jan. 27, 2010, now Pat. No. 8,287,482, which is a continuation of application No. 11/475,523, filed on Jun. 26, 2006, now Pat. No. 7,909,789.

(51) **Int. Cl.**
A61B 19/00 (2006.01)
A61F 9/007 (2006.01)

(52) **U.S. Cl.**
CPC **A61F 9/00781** (2013.01); **A61F 2210/0004** (2013.01); **A61F 2210/0014** (2013.01); **A61F 2250/0067** (2013.01)

(58) **Field of Classification Search**
CPC A61F 9/00781
USPC 604/8, 9, 264; 623/23.64, 23.7
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,159,161 A 12/1964 Ness
4,068,664 A 1/1978 Sharp et al.

4,457,757 A 7/1984 Moltano
4,553,545 A 11/1985 Maass et al.
4,719,825 A 1/1988 LaHaye et al.
4,936,825 A 6/1990 Ungerleider
4,957,505 A 9/1990 McDonald

(Continued)

FOREIGN PATENT DOCUMENTS

JP 2002-541976 A 12/2002
JP 2003-180730 A 7/2003

(Continued)

OTHER PUBLICATIONS

Boyle, E.L. (Feb. 1, 2006). "New Glaucoma Devices Take Different Approaches to IOP Lowering," *Ocular Surgery News U.S. Edition*, located at <<http://www.osnsupersite.com/view.aspx?rid=12436>>, last visited on Apr. 23, 2012, 4 pages.

(Continued)

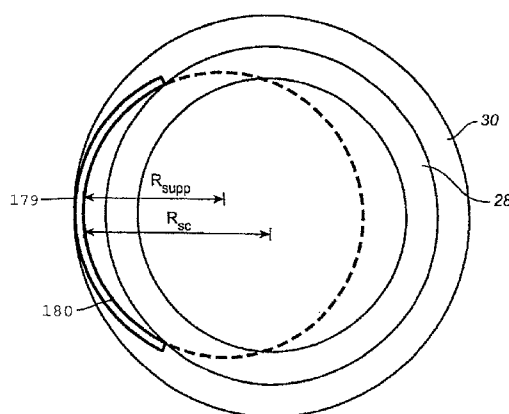
Primary Examiner — Leslie Deak

(74) *Attorney, Agent, or Firm* — Cooley LLP

(57) **ABSTRACT**

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmurial fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmurial fluid flow across the canal.

9 Claims, 15 Drawing Sheets



(56)

References Cited

U.S. PATENT DOCUMENTS

5,180,362 A 1/1993 Worst
 5,368,572 A 11/1994 Shiota
 5,486,165 A 1/1996 Stegmann
 5,569,197 A 10/1996 Helmus et al.
 5,626,558 A 5/1997 Suson
 5,639,278 A 6/1997 Dereume et al.
 5,868,697 A 2/1999 Richter et al.
 6,050,970 A 4/2000 Baerveldt
 6,299,603 B1 10/2001 Hecker et al.
 6,309,375 B1 10/2001 Glines et al.
 6,375,642 B1 * 4/2002 Grieshaber et al. 604/294
 6,494,857 B1 12/2002 Neuhaan
 6,508,779 B1 1/2003 Suson
 6,616,996 B1 9/2003 Keith et al.
 6,736,791 B1 5/2004 Tu et al.
 6,843,792 B2 1/2005 Nishtala et al.
 6,893,415 B2 5/2005 Madsen et al.
 7,207,980 B2 4/2007 Christian et al.
 7,331,984 B2 2/2008 Tu et al.
 7,909,789 B2 3/2011 Badawi et al.
 7,951,155 B2 5/2011 Smedley et al.
 7,967,772 B2 6/2011 McKenzie et al.
 8,075,511 B2 12/2011 Tu et al.
 8,287,482 B2 10/2012 Badawi et al.
 8,439,972 B2 5/2013 Badawi et al.
 8,491,549 B2 7/2013 Conston et al.
 8,529,622 B2 9/2013 Badawi et al.
 8,568,391 B2 10/2013 Kearns et al.
 8,876,898 B2 11/2014 Badawi et al.
 8,894,603 B2 11/2014 Badawi et al.
 9,095,412 B2 8/2015 Badawi et al.
 2002/0013546 A1 1/2002 Grieshaber et al.
 2002/0013572 A1 1/2002 Berlin
 2002/0133168 A1 9/2002 Smedley et al.
 2002/0143284 A1 10/2002 Tu et al.
 2003/0060447 A1 3/2003 Karakelle et al.
 2003/0060873 A1 3/2003 Gertner et al.
 2004/0044310 A1 3/2004 Suzuki
 2004/0193262 A1 * 9/2004 Shaddock 623/4.1
 2004/0254520 A1 12/2004 Porteous et al.
 2004/0254521 A1 12/2004 Simon
 2004/0260228 A1 12/2004 Lynch et al.
 2005/0055082 A1 3/2005 Ben Muvhar et al.
 2005/0171507 A1 8/2005 Christian
 2005/0267555 A1 12/2005 Marnfeldt et al.
 2005/0277864 A1 * 12/2005 Haffner et al. 604/8
 2006/0069340 A1 3/2006 Simon
 2006/0149194 A1 7/2006 Conston
 2006/0195187 A1 8/2006 Stegmann et al.
 2006/0200113 A1 9/2006 Haffner et al.
 2007/0073275 A1 3/2007 Conston et al.
 2007/0191863 A1 8/2007 De Juan, Jr. et al.
 2007/0276420 A1 11/2007 Sorensen et al.
 2008/0058760 A1 3/2008 Agerup
 2008/0082078 A1 4/2008 Berlin
 2008/0300574 A1 12/2008 Belson et al.
 2009/0036819 A1 2/2009 Tu et al.
 2009/0043321 A1 2/2009 Conston et al.
 2009/0132040 A1 5/2009 Frion et al.
 2009/0227934 A1 9/2009 Euteneuer et al.
 2010/0087774 A1 4/2010 Haffner et al.
 2010/0121248 A1 5/2010 Yu et al.
 2010/0173866 A1 7/2010 Hee et al.
 2010/0179652 A1 7/2010 Yamamoto et al.
 2010/0222802 A1 9/2010 Gillespie
 2011/0009874 A1 1/2011 Wardle et al.
 2011/0009958 A1 1/2011 Wardle et al.
 2011/0098809 A1 4/2011 Wardle et al.
 2011/0130831 A1 6/2011 Badawi et al.
 2011/0238009 A1 9/2011 Meron et al.
 2012/0136306 A1 5/2012 Bartha
 2012/0310072 A1 12/2012 Grieshaber
 2013/0041346 A1 2/2013 Alon
 2013/0158462 A1 6/2013 Wardle et al.
 2013/0253402 A1 9/2013 Badawi et al.

2013/0253438 A1 9/2013 Badawi et al.
 2013/0274655 A1 10/2013 Jennings et al.
 2014/0121584 A1 5/2014 Wardle et al.
 2015/0051699 A1 2/2015 Badawi et al.
 2015/0073328 A1 3/2015 Badawi et al.
 2015/0335481 A1 11/2015 Badawi et al.
 2016/0100980 A1 4/2016 Badawi et al.

FOREIGN PATENT DOCUMENTS

JP 2005-510317 A 4/2005
 JP 2005-538809 A 12/2005
 WO WO-00/64393 A1 11/2000
 WO WO-03/045582 A1 6/2003
 WO WO-2004/026361 A1 4/2004
 WO WO-2005/105197 A2 11/2005
 WO WO-2005/105197 A3 11/2005
 WO WO-2005/107664 A2 11/2005
 WO WO-2005/107664 A3 11/2005
 WO WO-2005/117752 A1 12/2005
 WO WO-2006/066103 A2 6/2006
 WO WO-2006/066103 A3 6/2006
 WO WO-2008/002377 A1 1/2008
 WO WO-2009/042596 A2 4/2009
 WO WO-2009/042596 A3 4/2009
 WO WO-2011/097408 A1 8/2011
 WO WO-2011/106781 A1 9/2011
 WO WO-2013/141898 A1 9/2013
 WO WO-2016/042162 A1 3/2016

OTHER PUBLICATIONS

Final Office Action mailed on Nov. 1, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 12 pages.
 Final Office Action mailed on Jul. 19, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 6 pages.
 Final Office Action mailed on Feb. 1, 2013, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 6 pages.
 Final Office Action mailed on Sep. 15, 2014, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 13 pages.
 International Search Report mailed on Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, 4 pages.
 International Search Report mailed on Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 2 pages.
 Non-Final Office Action mailed on May 17, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 10 pages.
 Non-Final Office Action mailed on Jan. 26, 2012, for U.S. Appl. No. 12/695,053, filed Jan. 27, 2010, 10 pages.
 Non-Final Office Action mailed on Mar. 15, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 4 pages.
 Non-Final Office Action mailed on May 11, 2012, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 5 pages.
 Non-Final Office Action mailed on Nov. 9, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 5 pages.
 Non-Final Office Action mailed on Feb. 24, 2014, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 12 pages.
 Notice of Allowance mailed on Feb. 2, 2011, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 6 pages.
 Notice of Allowance mailed on Jun. 11, 2012, for U.S. Appl. No. 12/695,053, filed Jan. 27, 2010, 7 pages.
 Notice of Allowance mailed on Apr. 2, 2013, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 6 pages.
 Notice of Allowance mailed on May 10, 2013, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 8 pages.
 Notice of Allowance mailed on Jul. 7, 2014, for U.S. Appl. No. 14/012,963, filed Aug. 28, 2013, 6 pages.
 Restriction Requirement mailed on Sep. 30, 2009, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 9 pages.
 Restriction Requirement mailed on Feb. 23, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 6 pages.
 Restriction Requirement mailed on Mar. 28, 2012, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 7 pages.

(56)

References Cited**OTHER PUBLICATIONS**

Written Opinion mailed on Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, 6 pages.

Written Opinion mailed on Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 5 pages.

U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, by Badawi et al.

Final Office Action mailed on Apr. 23, 2015, for U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 8 pages.

Non-Final Office Action mailed on Feb. 23, 2015, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 17 pages.

European Search Report mailed Apr. 22, 2015, for EP Patent Application No. 11740372.5, filed Feb. 3, 2011, six pages.

Final Office Action mailed on Sep. 20, 2013, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 16 pages.

Final Office Action mailed on Nov. 12, 2013, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 8 pages.

Final Office Action mailed on Jan. 8, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 8 pages.

Final Office Action mailed on Sep. 3, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 8 pages.

International Search Report mailed on Feb. 1, 2013 for PCT Application No. PCT/US2012/058751, filed on Oct. 4, 2012, 4 pages.

International Search Report mailed on Sep. 14, 2015, for PCT Application No. PCT/US2015/023720, filed on Mar. 31, 2015, 16 pages.

Non-Final Office Action mailed on Apr. 24, 2013, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 13 pages.

Non-Final Office Action mailed on Jun. 12, 2013, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 8 pages.

Non-Final Office Action mailed on Sep. 9, 2013, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.

Non-Final Office Action mailed on Feb. 7, 2014, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 12 pages.

Non-Final Office Action mailed on May 15, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.

Non-Final Office Action mailed on Nov. 28, 2014, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 7 pages.

Non-Final Office Action mailed on Jan. 14, 2015, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 10 pages.

Non-Final Office Action mailed on Feb. 4, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 6 pages.

Non-Final Office Action mailed on Jul. 10, 2015, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 16 pages.

Non-Final Office Action mailed on Oct. 7, 2015, U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 5 pages.

Non-Final Office Action mailed on Nov. 3, 2015, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 7 pages.

Notice of Allowance mailed on Jul. 23, 2014, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 8 pages.

Notice of Allowance mailed on Mar. 30, 2015, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 5 pages.

Notice of Allowance mailed on Aug. 10, 2015, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.

Restriction Requirement mailed on Sep. 25, 2015, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 6 pages.

Written Opinion mailed on Feb. 1, 2013 for PCT Application No. PCT/US2012/058751, filed on Oct. 4, 2012, 6 pages.

Written Opinion mailed on Sep. 14, 2015 for PCT/US2015/023720, filed on Mar. 31, 2015, 8 pages.

Final Office Action mailed on Mar. 9, 2016, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 11 pages.

Non-Final Office Action mailed on Feb. 25, 2016, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 19 pages.

Final Office Action mailed on Jun. 7, 2016, for U.S. Appl. No. 14/527,292, filed Oct. 10, 2014, 5 pages.

Japanese Office Action mailed on Mar. 16, 2016 for Japanese Patent Application No. 2014-152575, filed on May 31, 2007, 3 pages (4 pages translation).

Notice of Allowance mailed on Mar. 1, 2016, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 7 pages.

Corrected Notice of Allowability mailed on Apr. 25, 2016, U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 2 pages.

Supplementary European Search Report mailed on Mar. 24, 2016, for European Patent Application No. 12871982.0, filed on Oct. 4, 2012, 7 pages.

Extended European Search Report mailed on Jun. 9, 2016, for European Patent Application No. 16 155 079.3, filed on May 31, 2007, 7 pages.

* cited by examiner

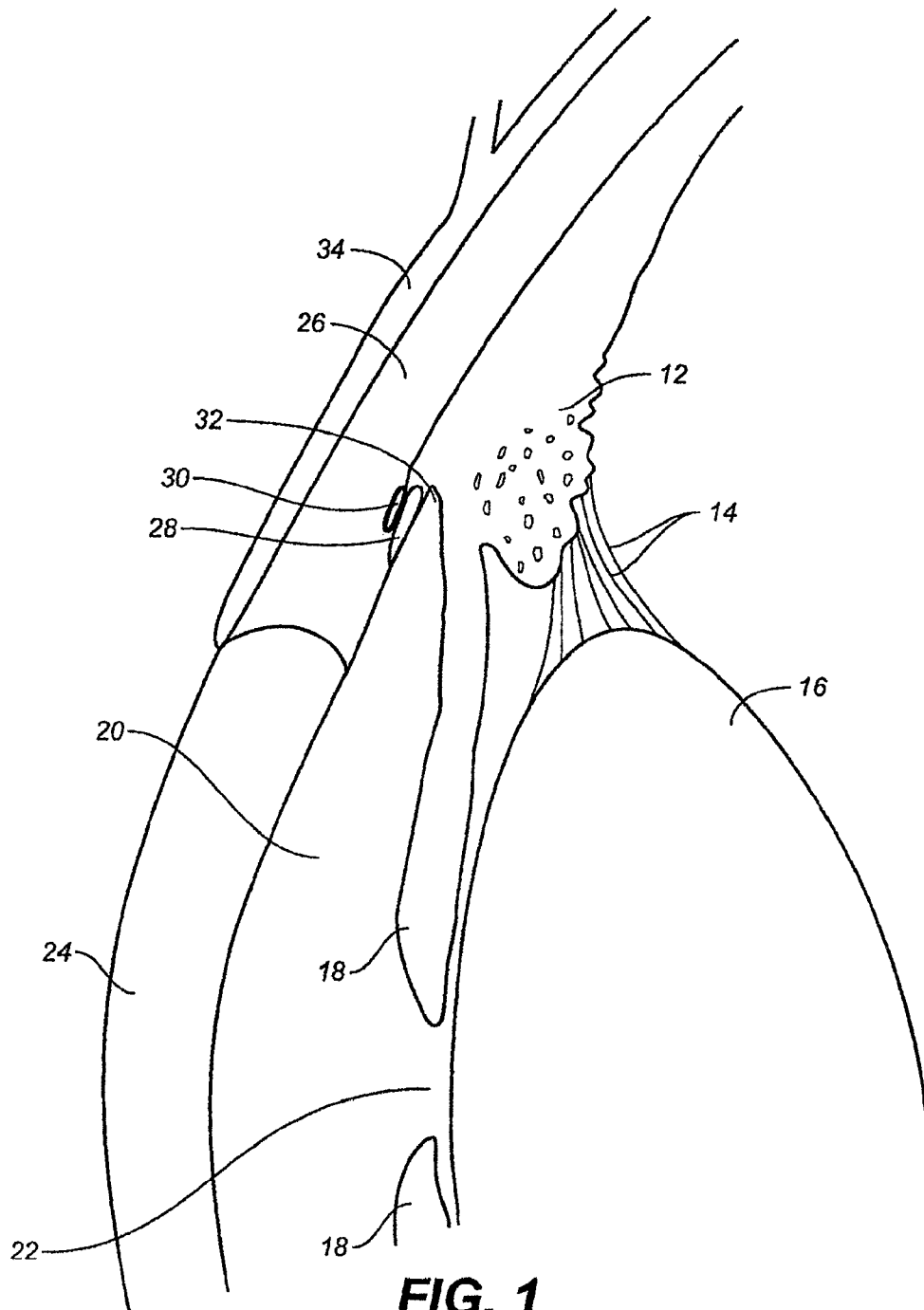
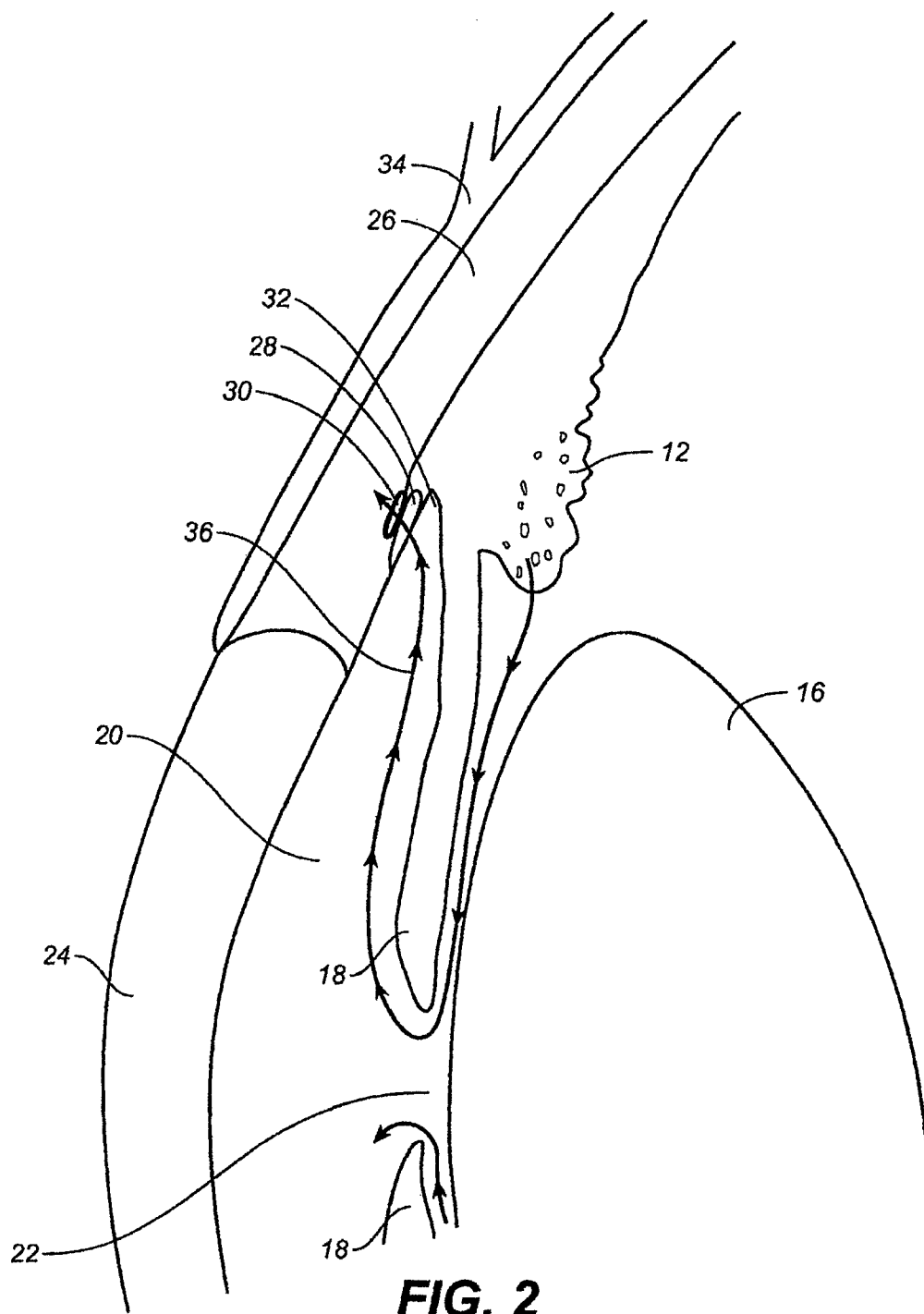


FIG. 1



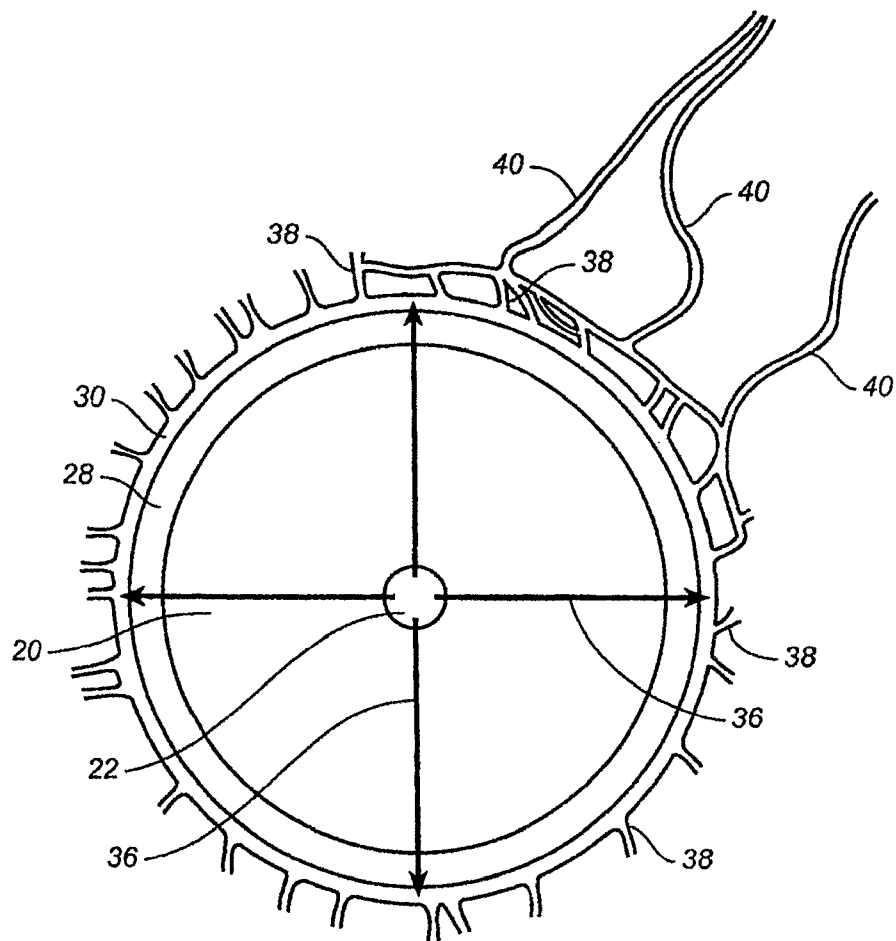


FIG. 3

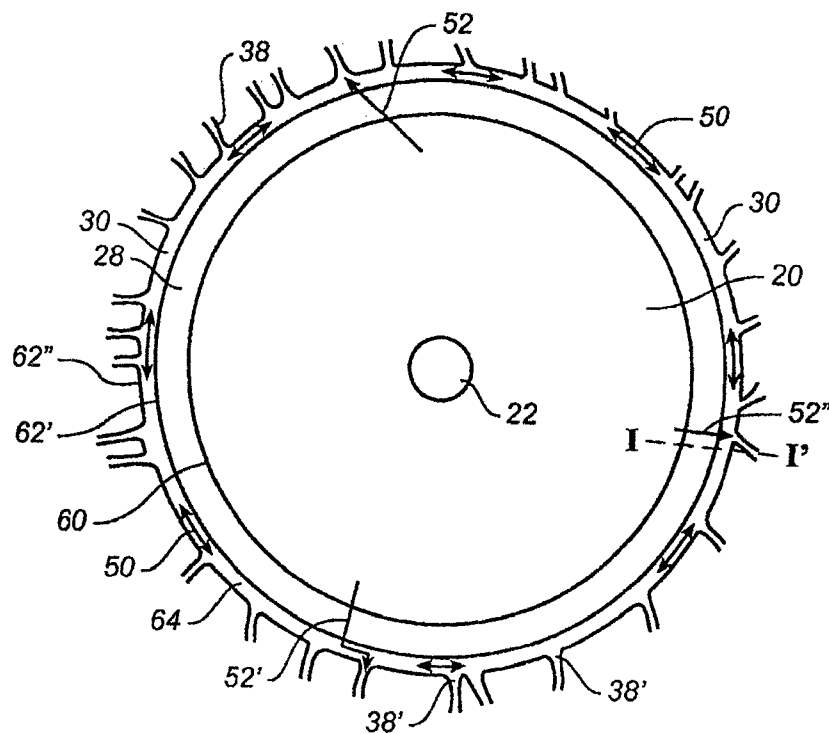


FIG. 4A

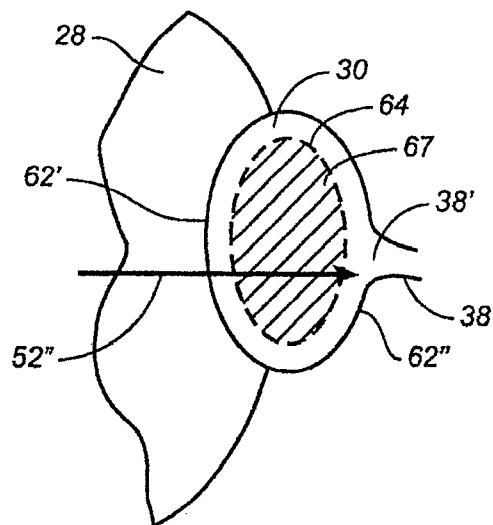


FIG. 4B

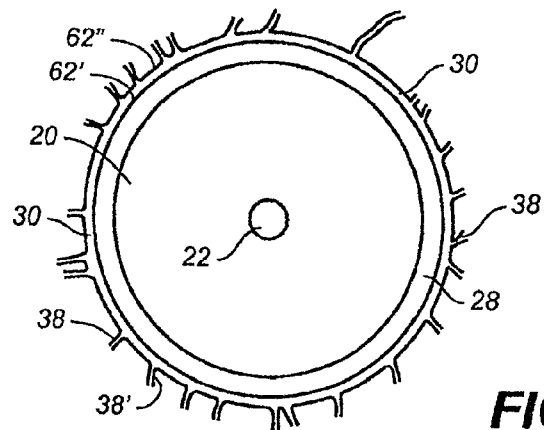


FIG. 5A

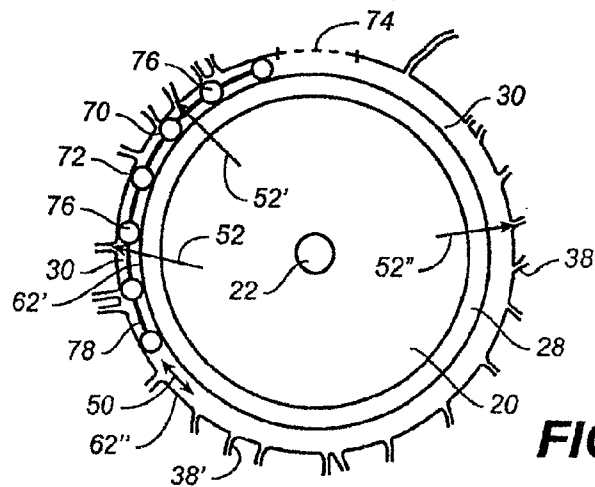


FIG. 5B

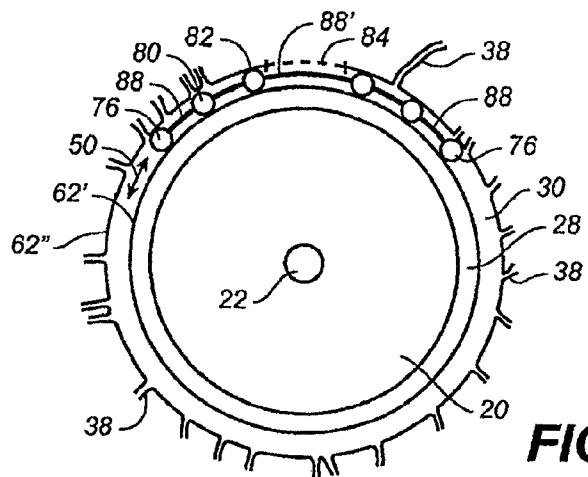


FIG. 5C

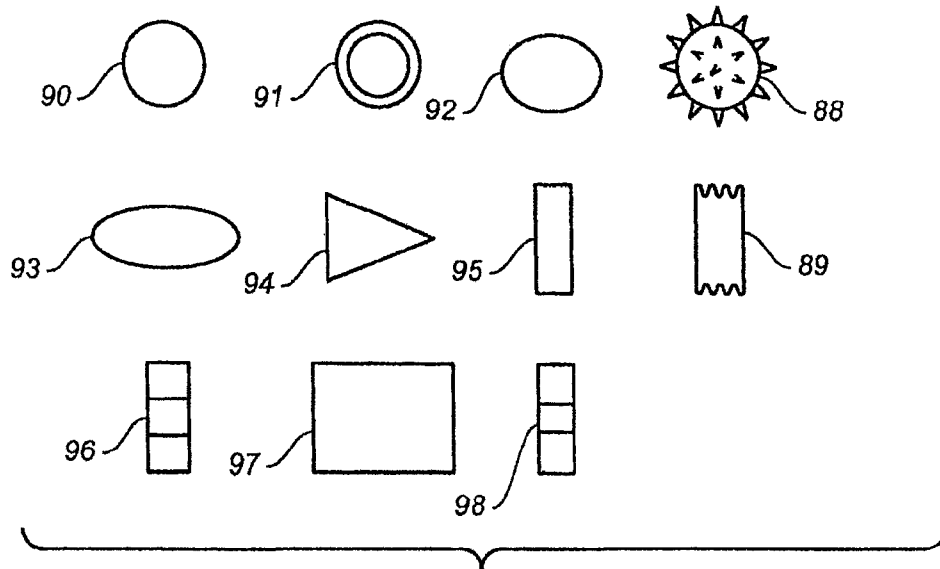


FIG. 6A

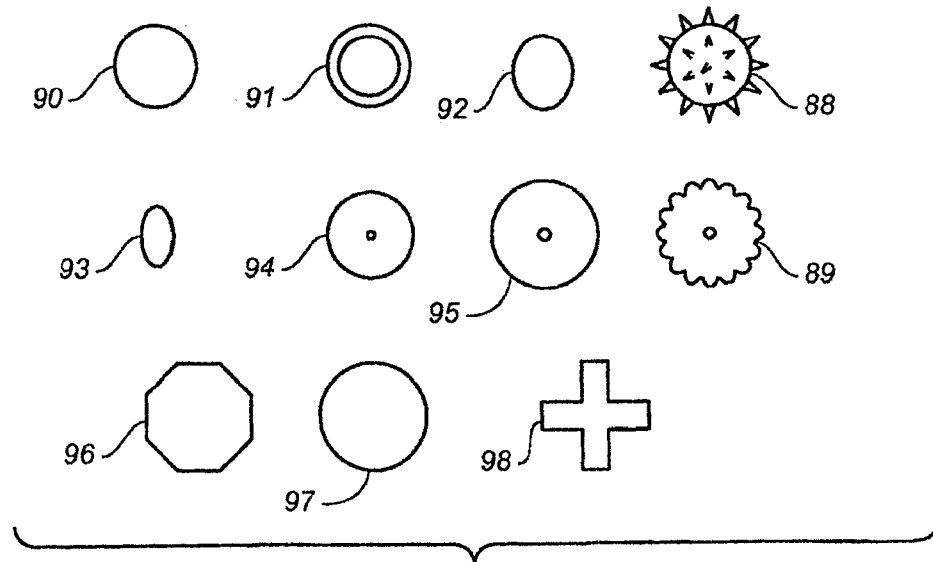


FIG. 6B

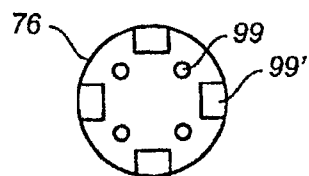


FIG. 6C



FIG. 7A



FIG. 7B

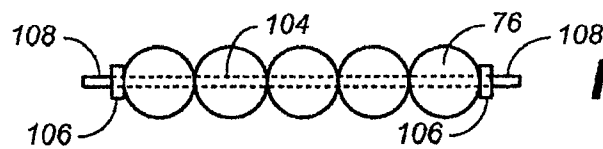


FIG. 7C

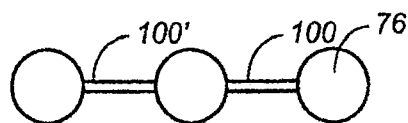


FIG. 7D

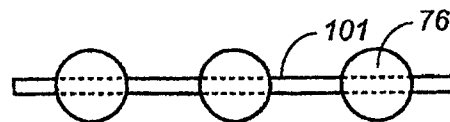


FIG. 7E

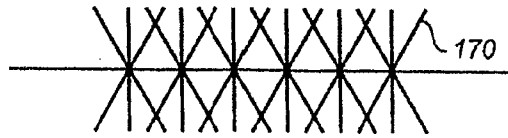


FIG. 8A

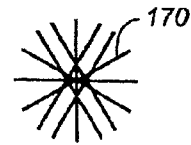


FIG. 8B

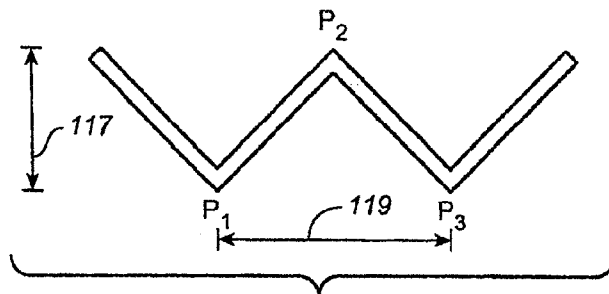


FIG. 8C



FIG. 8D

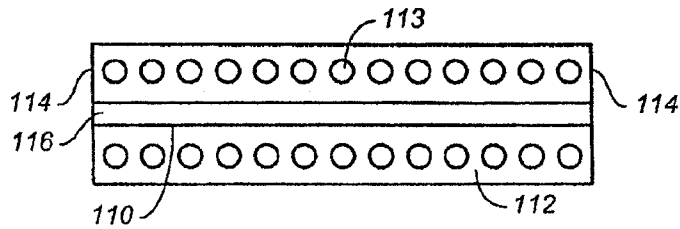


FIG. 8E

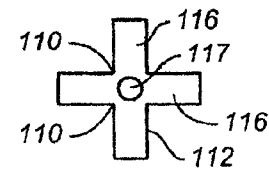


FIG. 8F

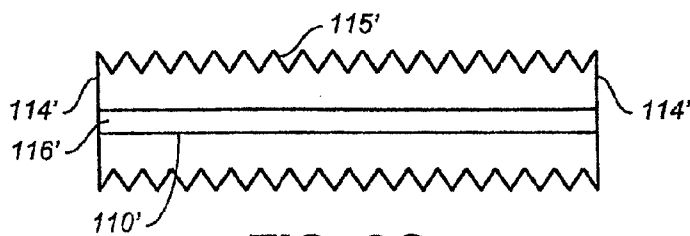


FIG. 8G

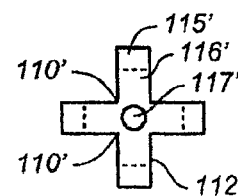


FIG. 8H

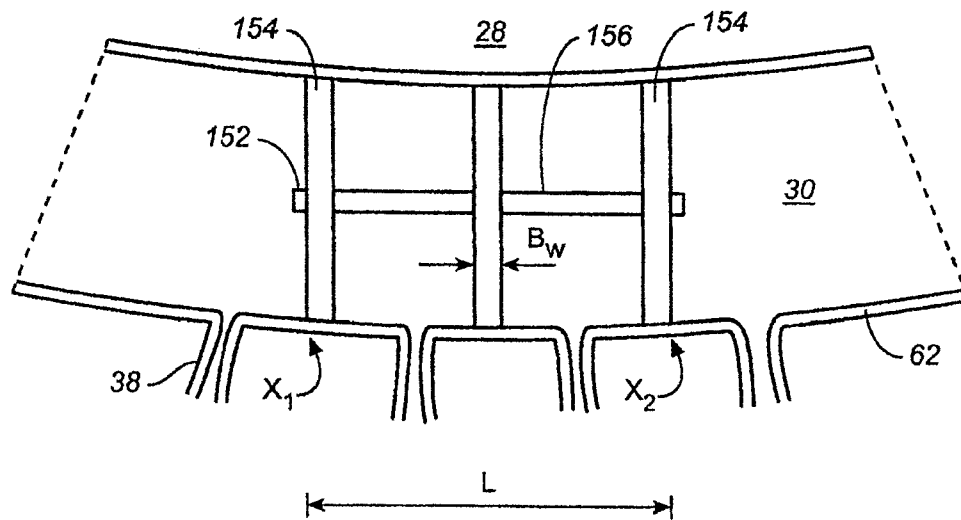


FIG. 9A

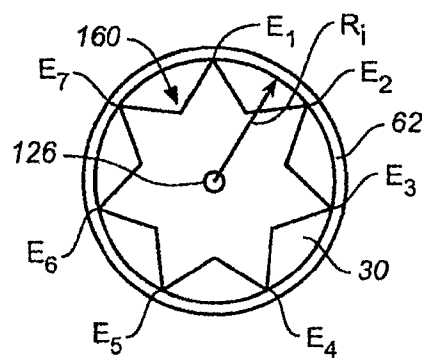


FIG. 9B

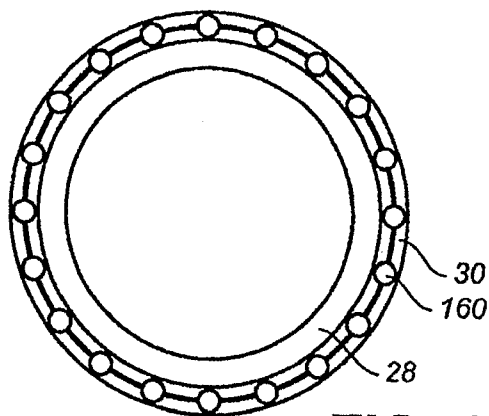


FIG. 10A

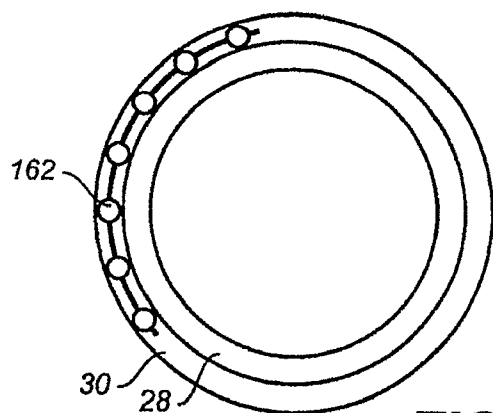


FIG. 10B

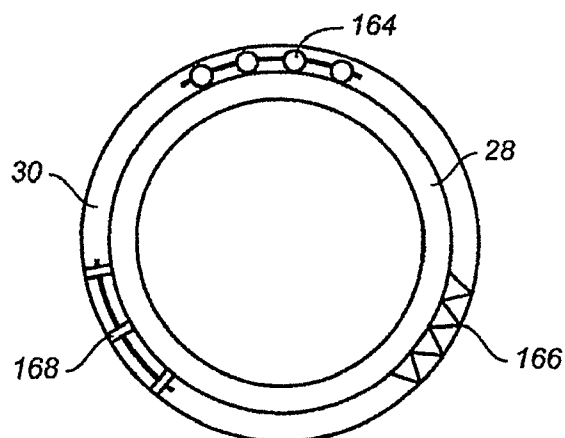
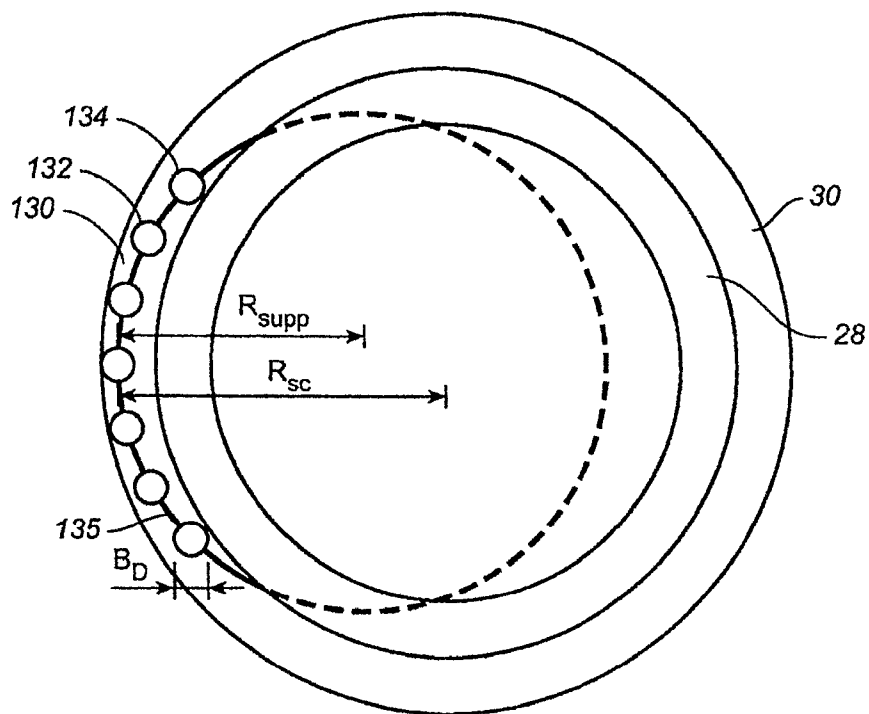


FIG. 10C

**FIG. 11A**

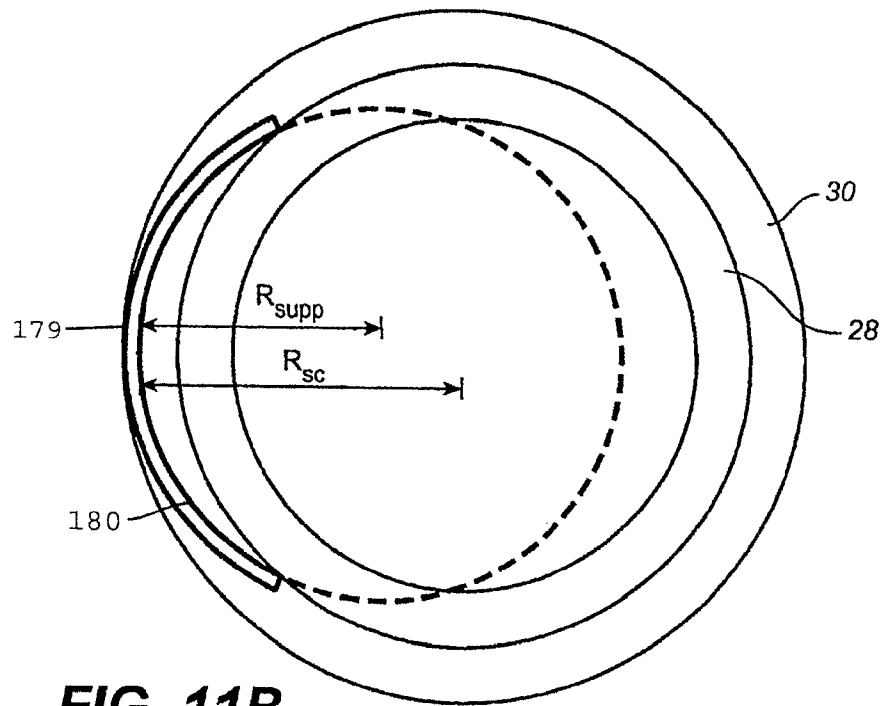


FIG. 11B

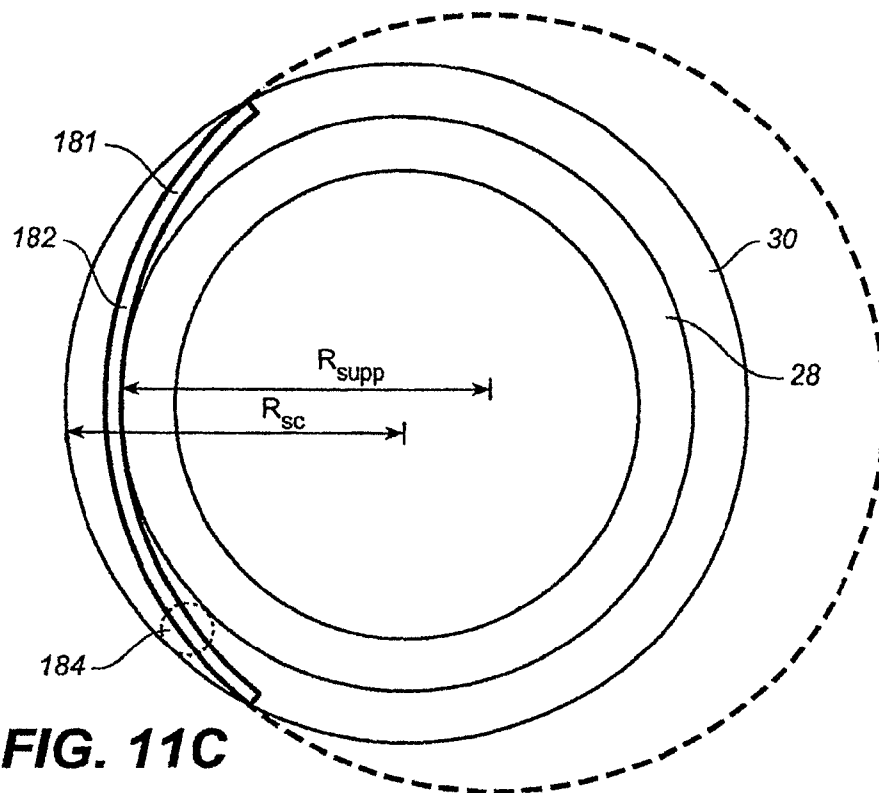


FIG. 11C

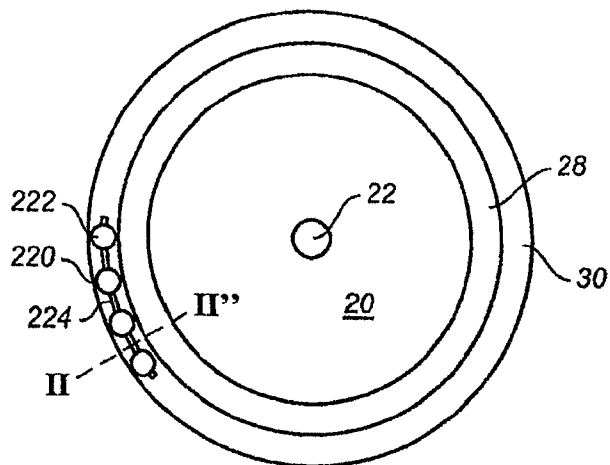


FIG. 12A

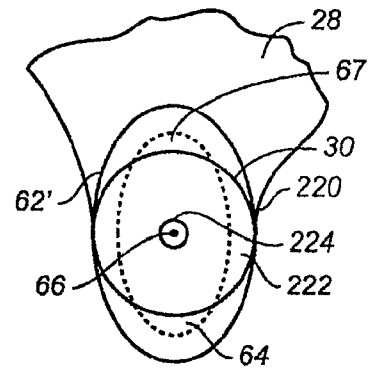


FIG. 12B

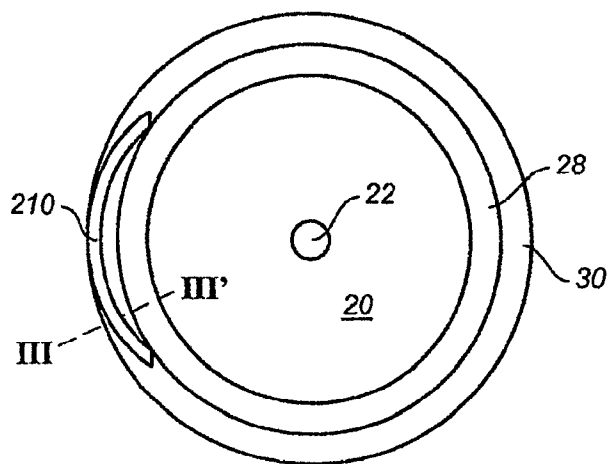


FIG. 12C

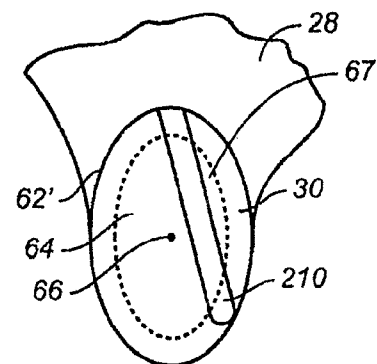


FIG. 12D

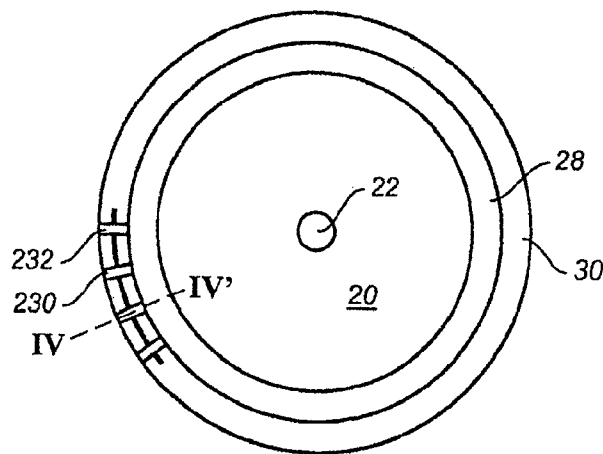


FIG. 12E

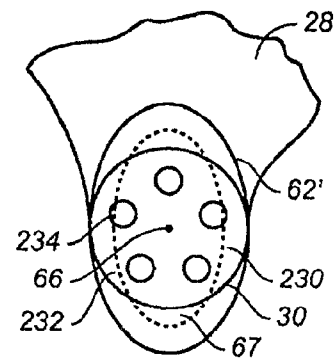


FIG. 12F

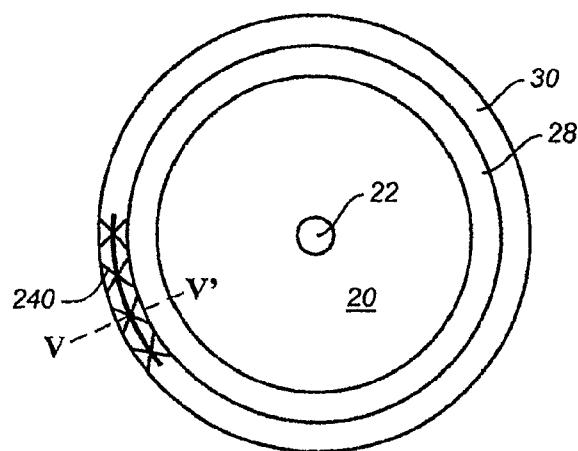


FIG. 12G

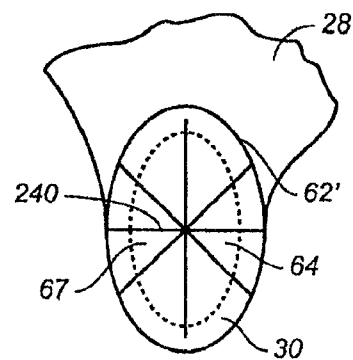


FIG. 12H

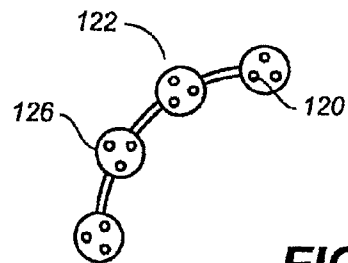


FIG. 13

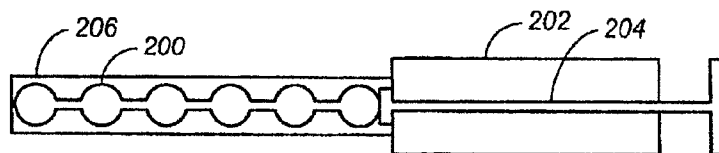


FIG. 14A

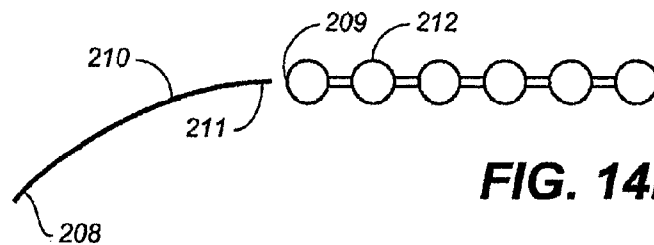


FIG. 14B



FIG. 14C

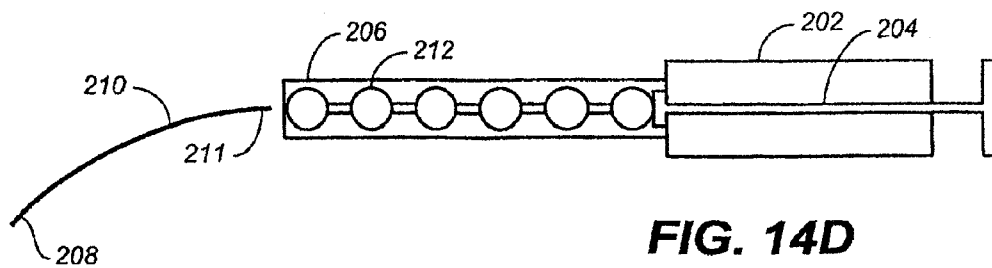


FIG. 14D

1

INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 12/695,053, filed Jan. 27, 2010, which is a continuation of U.S. patent application Ser. No. 11/475,523, filed on Jun. 26, 2006 (now U.S. Pat. No. 7,909,789), the disclosures of which are hereby incorporated by reference in their entirety.

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical

2

therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjunctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmural flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal. The support does not substantially interfere with transmural flow across Schlemm's canal, and thereby uti-

lizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocompatible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer; a polyorthoester; a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a poly-anhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, cubical, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted between three beads, the connectors may be of the same or different lengths. The connectors can include the same or

different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmurial flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can include implanting at least two supports. If more than one support is implanted within a single eye, the multiple

5

supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 provides a partial cross-sectional side view of a normal human eye.

FIG. 2 provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. 3 shows a front view of normal fluid drainage from the eye.

FIG. 4A shows an alternative front view of normal fluid drainage paths from the eye. FIG. 4B shows a cross-sectional view along line I-I'.

FIG. 5A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. 5B shows a front view of a device including a support inserted into Schlemm's canal that allows transmural flow across the canal. FIG. 5C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmural flow across the canal.

FIG. 6A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. 6B shows the corresponding front views of the element or bead configurations shown in FIG. 6A. FIG. 6C illustrates an element or bead having fenestrations.

FIG. 7A illustrates a support having multiple juxtaposed beads. FIG. 7B illustrates a support having multiple juxtaposed and connected beads. FIG. 7C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. 7D shows a support having multiple, spaced-apart but connected beads. FIG. 7E illustrates beads threaded onto a connector.

FIGS. 8A-B show side and front views, respectively, of a support having an open network structure. FIGS. 8C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at least three points (labeled P₁, P₂, P₃). FIGS. 8E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. 8G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. 9A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. 10A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. 11A-B illustrate two configurations of supports having a smaller radius of curvature than Schlemm's canal. FIG. 11C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. 12A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. 12B shows a cross-sectional view along line II-II'. FIG. 12C illustrates a variation of a support traversing the central core

6

of the canal. FIG. 12D shows a cross-sectional view along line III-III'. FIG. 12E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. 12F shows a cross-sectional view along line IV-IV'. FIG. 12G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. 12H shows a cross-sectional view along line V-V'.

FIG. 13 shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. 14A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. 14B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. 14C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. 14D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmural fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. 1 shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body 12 is connected to iris 18 and to lens 16 via zonular fibrils 14. The anterior chamber of the eye 20 is bounded on its anterior (front) surface by cornea 24. In the center of iris 18 is pupil 22. Cornea 24 is connected on its periphery to sclera 26, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork 28 is located on the outer peripheral surface of anterior chamber 20. The trabecular meshwork extends 360° circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork 28 is Schlemm's canal 30. Schlemm's canal extends 360° circumferentially around the trabecular meshwork. At the apex formed between iris 18, meshwork 28 and sclera 26 is angle 32. Conjunctiva 34 is a membrane overlaying sclera 26 and lining the inside of the eyelid (not shown).

FIG. 2 shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body 12 and its path through and out of the eye is indicated by solid directional line 36. The aqueous humor flows from ciliary body 12, between lens 16 and iris 18, through pupil 22 into anterior chamber 20, across trabecular meshwork 28, across Schlemm's canal 30, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. 3 shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber 20 via pupil 22. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines 36. The fluid crosses trabecular meshwork 28 and traverses Schlemm's canal 30 to reach aqueous veins or collector channels 38. There are typically 25-30 collector channels located in a human eye. Collector channels 38 are connected to vasculature 40, whereby the drained aqueous humor enters the bloodstream. Although

the direction of net or bulk fluid flow is depicted as radially outward by directional lines 36 from pupil 22 for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. 4A-B. FIG. 4A shows a front view of an eye, and FIG. 4B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal 30 is depicted by directional lines 50. Fluid that does not traverse canal 30 to reach collector channels 38 may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines 52, 52', and 52". In each of these paths, fluid enters trabecular meshwork 28 along its inner peripheral surface 60 and exits the meshwork along its outer peripheral surface 62'. Meshwork outer peripheral surface 62' provides the inner peripheral surface or wall of Schlemm's canal 30. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork 38 through inner peripheral surface or wall 62' of Schlemm's canal 30 to reach lumen 64 of the canal. Second, fluid must flow from lumen 64 through canal outer peripheral wall 62" through apertures 38' to enter collector channels 38. Finally, the collector channels 38 feed the drained fluid into vasculature. Lumen 64 of canal 30 includes a central core region 67. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflow from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1) fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral bound-

ary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the connector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. 5A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal 30, where canal outer peripheral wall 62" is very close to canal inner peripheral wall 62'. Although Schlemm's canal 30 is depicted in FIG. 5A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels 38 is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. 5B illustrates an example of a device 70 inserted into Schlemm's canal 30 through incision site 74. Device 70 in this example is positioned to one side of incision site 74. Device 70 includes support 72 that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall 62' and canal outer wall 62" to reach collector channels 38 via apertures 38'. In the example shown in FIG. 5B, support 72 includes elements or beads 76 connected with connectors 78. In this variation, the distance between canal inner wall 62' and outer wall 62" is approximately determined by the cross-sectional dimension of support 72, which is in turn determined by the largest cross-sectional diameter of the beads 76. Therefore, circumferential (i.e., longitudinal) fluid flow around and along the canal 30 indicated by directional line 50 may be inhibited by

the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52''** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters (e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. 5C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. 5B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. 6A and 6B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges, **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. 6C, elements or beads **76** may include fenestrations **99**, **99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. 6C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. 7A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. 7A), connected and juxtaposed (FIGS. 7B and 7C), or connected together with connectors **100**, **100'** to form intervals between beads (FIG. 7D). In addition, beads may be threaded onto a connector **101** (FIG. 7E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. 7B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. 7C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knot-

ting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. 7D, multiple connectors **100**, **100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100**, **100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100**, **100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. 7E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100**, **100'**, **101** can be flexible, such as thin polymer threads or metal wires. Connectors **100**, **100'**, **101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100**, **100'**, **101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. 8A-F. As illustrated in FIG. 8A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. 8A-B will have minimal surface area contact with the walls of Schlemm's canal, i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. 8C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. 8C, the support will contact the wall of Schlemm's canal at least three points, labeled P_1 , P_2 , and P_3 , after implantation. In FIGS. 8E-H, examples of rod-like supports having fluted edges are shown. In FIGS. 8E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include fenestrations **113**. The support can include central bore **117**. In FIGS. 8G-H, fluted edges **110'** extend along sides **112'** to

11

form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. **8E-H**, the support may contact the canal walls at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. **8A-B** shows, some supports only have point contacts with the canal wall. For the supports shown in FIGS. **5B-C**, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. **6A-B** may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. **7D-E** that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. **8C-D**, in some variations, the support contacts the interior wall of the canal at least two points; or at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided FIGS. **9A-B**. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder **C** having length **L**, extending circumferentially from a first end **X₁** to a second end **X₂** of support **152**, and inside radius **R_i**. In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder **C** as described above. In other variations, the support contacts less than 10% of the surface area of **C**. In still other variations, the support contacts less than 30% of the surface area of **C**. For example, the support **152** shown in FIGS. **9A-B** contacts the canal wall **62** only at bead outer peripheral edges at **E₁-E₇**, along a distance of the bead width **B_w**. There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmurial flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapeable metal having a sinusoidal or zig-zag configuration as shown FIGS. **8C-D**, a cross-sectional dimension **117** of the support can be decreased or increased by apply tension along dimension **119**. As illustrated in FIG. **10A**, a support **160** can extend essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately half way around the circumference of the canal (not shown).

12

As shown in FIG. **10B**, a support **162** can extend less than half way around the canal. As shown in FIG. **10C**, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. **11A**, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension **B_D**. Support **132** comprises a stiff arcuate element **135** with a radius of curvature **R_{supp}** smaller than the radius of curvature of Schlemm's canal **R_{SC}**. The smaller, fixed radius of curvature **R_{supp}** of arcuate member **135** urges canal **30** to open more than **B_D**. In another variation shown in FIG. **11B**, support **179** comprises an arcuate member **180** without beads having a radius of curvature **R_{supp}** that is less than the radius of curvature **R_{SC}** of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. **11C**, support **181** comprises an arcuate member **182** having a radius of curvature **R_{supp}** larger than that of Schlemm's canal **R_{SC}**. Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. **11C**, support **181** can include beads **184**. To urge open the canal, the radius of curvature **R_{supp}** of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal **R_{SC}**. For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member **R_{supp}** in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature **R_{supp}** of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at least one point. Referring to FIG. **12A**, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. **12B** shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. **12C**, a front view of an arcuate support **210** is shown. FIG. **12D** shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. **12E**, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. **12F**. As illustrated in FIG. **12F**, bead **232** with fenestrations **234** occupies the majority of central core **67** of canal **30**. In other variations, the support occupies only a small portion of the central core of the canal.

For example, in FIG. 12G, a front view of a support 240 having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. 12H.

A support can be made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacrylate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives, flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly(lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly(ethylene glycol) copolymer, a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer, a poly(lactic acid)/poly(ethylene glycol) copolymer, a poly(glycolic acid)/poly(ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone)/poly(ethylene glycol) copolymer, a polyorthoester, a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a poly(anhydride), a poly(dioxanone), a poly(alkylene alkylate), a copolymer of polyethylene glycol and a polyorthoester, a biodegradable polyurethane, a poly(amino acid), a polyetherester, a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(e-caprolactone) dimethacrylate and n-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins,

prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. 13, predetermined localized portions 120 of support 122 can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions 120 will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads 126 in support 120 are hollow, then after irradiation and ablation, features 120 will become fenestrations. The fenestrations can be created to make support 122 more porous in nature or to allow release of an active agent from within a support, e.g., from within beads 126. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength

15

range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminescent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the support may be allowed to self-position in Schlemm's canal. In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

FIGS. 14A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. 14A, a support 200 can be introduced into the canal using syringe 202 and plunger 204. Syringe 202 has distal end 206 that can be at least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger

16

204, thereby pushing support 200 into the canal. Referring to FIGS. 14B-C, distal end 208 of guide element 210 can be at least partially introduced into the canal. Guide element 210 can be a guide wire. Guide element 210 can be extended circumferentially along the canal to aid in positioning the support. Support 212 comprises central bore 218 capable of accommodating guide element 210 such that support 212 can be threaded onto guide element 210 and slidably positioned along the guide element. Once distal end 209 of support 212 is threaded onto guide element 210, support 212 can be pushed in a distal direction along guide element 210 to insert support 212 into the canal. In some variations, support 212 can remain threaded onto guide element 210, and guide element 210 can remain in the canal. In other variations, support 212 can be slid off distal end 208 of guide element 210, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. 14C-D, syringe 202 with plunger 204 can be used in combination with a guide element 210. In this variation, distal end 208 of guide element 210 is inserted at least partially into Schlemm's canal. Guide element 210 can be extended circumferentially along the canal to aid in positioning the support. Support 212 has central bore 218 capable of accommodating guide element 210. Proximal end 211 of guide element 210 is inserted into bore 218. Plunger 204 is depressed in a distal direction to push support 212 into the canal and slide support 212 along element 210. Guide element 210 can remain in the canal or be removed following insertion of the support. Supports 200, 212 must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In

addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more mirrors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of

ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. 11A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

What we claim is:

1. A method for reducing intraocular pressure, comprising:

introducing a tubular cannula having a lumen at least partially within Schlemm's canal;

delivering a high viscosity fluid into Schlemm's canal; and

inserting a support into Schlemm's canal by passing the support through the tubular cannula, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than a radius of curvature of Schlemm's canal, and wherein the support comprises at least one fenestration.

2. The method of claim 1, wherein the delivered fluid dilates the canal.

3. The method of claim 1, wherein the high viscosity fluid is sodium hyaluronate.

4. The method of claim 1, wherein the support is a rigid support.

5. The method of claim 1, wherein the support contacts the interior wall of the canal at least at three points.

6. The method of claim 1, wherein the support does not substantially interfere with longitudinal flow along the canal.

7. The method of claim 1, wherein the support does not substantially interfere with transmural flow across the inner wall of the canal.

8. The method of claim 1, wherein the support does not substantially interfere with transmural flow across the outer wall of the canal.

9. The method of claim 1, wherein at least a portion of the support extends out of Schlemm's canal and into the trabecular meshwork.

EXHIBIT D

US010314742B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.:** **US 10,314,742 B2**
(45) **Date of Patent:** ***Jun. 11, 2019**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

(71) Applicant: **Sight Sciences, Inc.**, Menlo Park, CA (US)

(72) Inventors: **David Y. Badawi**, Glenview, IL (US);
Paul Badawi, Menlo Park, CA (US)

(73) Assignee: **Sight Sciences, Inc.**, Menlo Park, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 329 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/182,165**

(22) Filed: **Jun. 14, 2016**

(65) **Prior Publication Data**

US 2016/0287440 A1 Oct. 6, 2016

Related U.S. Application Data

(60) Continuation of application No. 13/025,112, filed on Feb. 10, 2011, now Pat. No. 9,370,443, which is a (Continued)

(51) **Int. Cl.**
A61F 9/00 (2006.01)
A61F 9/007 (2006.01)

(52) **U.S. Cl.**
CPC **A61F 9/00781** (2013.01); **A61F 9/0017** (2013.01); **A61F 2210/0004** (2013.01); (Continued)

(58) **Field of Classification Search**
CPC A61F 9/00781; A61F 2210/0014; A61F 2250/0067 (Continued)

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,159,161 A 12/1964 Ness
4,068,664 A 1/1978 Sharp et al.
(Continued)

FOREIGN PATENT DOCUMENTS

JP 2002-541976 A 12/2002
JP 2003-180730 A 7/2003
(Continued)

OTHER PUBLICATIONS

Boyle, E.L. (Feb. 1, 2006). "New Glaucoma Devices Take Different Approaches to IOP Lowering," *Ocular Surgery News U.S. Edition*, located at <<http://www.osnsupersite.com/view.aspx?rid=12436>>, last visited on Apr. 23, 2012, 4 pages, revisited on Apr. 19, 2016, 5 pages.

(Continued)

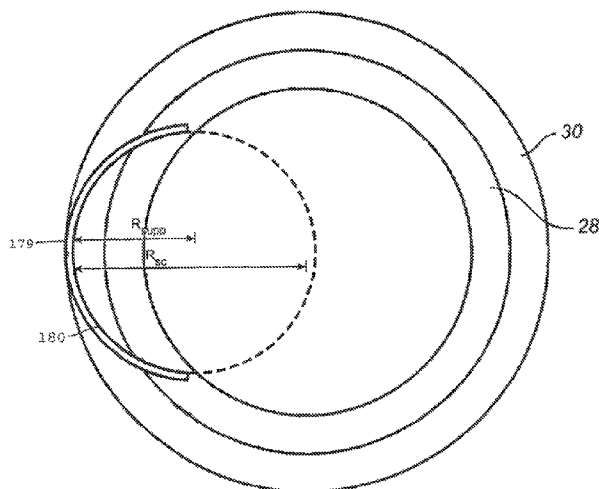
Primary Examiner — Leslie R Deak

(74) *Attorney, Agent, or Firm* — Cooley LLP

(57) **ABSTRACT**

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmurial fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmurial fluid flow across the canal.

20 Claims, 16 Drawing Sheets



US 10,314,742 B2

Page 2

Related U.S. Application Data

division of application No. 11/475,523, filed on Jun. 26, 2006, now Pat. No. 7,909,789.

(52) **U.S. Cl.**

CPC A61F 2210/0014 (2013.01); A61F 2250/0067 (2013.01)

(58) **Field of Classification Search**

USPC 604/8, 9, 264; 623/23.64, 23.7
See application file for complete search history.

(56)

References Cited

U.S. PATENT DOCUMENTS

4,457,757 A	7/1984	Molteno	8,034,105 B2	10/2011	Stegmann et al.
4,501,274 A	2/1985	Skjaerpe	8,075,511 B2	12/2011	Tu et al.
4,553,545 A	11/1985	Maass et al.	8,109,896 B2	2/2012	Nissan et al.
4,719,825 A	1/1988	LaHaye et al.	8,123,729 B2	2/2012	Yamamoto et al.
4,936,825 A	6/1990	Ungerleider	8,133,208 B2	3/2012	Hetherington
4,957,505 A	9/1990	McDonald	8,152,752 B2	4/2012	Lynch et al.
5,092,837 A	3/1992	Ritch et al.	8,172,899 B2	5/2012	Silvestrini et al.
5,180,362 A	1/1993	Worst	8,267,882 B2	9/2012	Euteneuer et al.
5,284,476 A	2/1994	Koch	8,273,050 B2	9/2012	Bergheim et al.
5,358,473 A	10/1994	Mitchell	8,282,592 B2	10/2012	Schieber et al.
5,360,399 A	11/1994	Stegmann	8,287,482 B2	10/2012	Badawi et al.
5,368,572 A	11/1994	Shirota	8,333,742 B2	12/2012	Bergheim et al.
5,486,165 A	1/1996	Stegmann	8,337,509 B2	12/2012	Schieber et al.
5,540,657 A	7/1996	Kurjan et al.	8,348,924 B2	1/2013	Christian et al.
5,558,634 A	9/1996	Mitchell	8,366,653 B2	2/2013	Shareef et al.
5,569,197 A	10/1996	Helmus et al.	8,372,026 B2	2/2013	Schieber et al.
5,626,558 A	5/1997	Suson	8,388,568 B2	3/2013	Lynch et al.
5,639,278 A	6/1997	Dereume et al.	8,403,920 B2	3/2013	Lind et al.
5,792,099 A	8/1998	DeCamp et al.	8,414,518 B2	4/2013	Schieber et al.
5,792,103 A	8/1998	Schwartz et al.	8,425,449 B2	4/2013	Wardle et al.
5,868,697 A	2/1999	Richter et al.	8,425,450 B2	4/2013	Wilcox
6,036,678 A	3/2000	Giungo	8,439,972 B2	5/2013	Badawi et al.
6,050,970 A	4/2000	Baerveldt	8,444,589 B2	5/2013	Silvestrini
6,050,999 A	4/2000	Paraschac et al.	8,491,549 B2	7/2013	Conston et al.
6,299,603 B1	10/2001	Hecker et al.	8,512,321 B2	8/2013	Baerveldt et al.
6,309,375 B1	10/2001	Glines et al.	8,512,404 B2	8/2013	Frion et al.
6,375,642 B1	4/2002	Grieshaber et al.	8,529,622 B2	9/2013	Badawi et al.
6,491,670 B1	12/2002	Toth et al.	8,540,659 B2	9/2013	Berlin
6,494,857 B1	12/2002	Neuhann	8,540,681 B2	9/2013	Hetherington
6,508,779 B1	1/2003	Suson	8,545,431 B2	10/2013	Rickard
6,524,275 B1	2/2003	Lynch et al.	8,568,391 B2	10/2013	Kearns et al.
6,533,768 B1	3/2003	Hill	8,617,094 B2	12/2013	Smedley et al.
6,616,996 B1	9/2003	Keith et al.	8,657,776 B2	2/2014	Wardle et al.
6,626,858 B2	9/2003	Lynch et al.	8,663,150 B2	3/2014	Wardle et al.
6,666,841 B2	12/2003	Gharib et al.	8,715,266 B2	5/2014	Bos
6,726,676 B2	4/2004	Stegmann et al.	8,734,377 B2	5/2014	Schieber et al.
6,730,056 B1	5/2004	Ghaem et al.	8,747,299 B2	6/2014	Grieshaber
6,736,791 B1	5/2004	Tu et al.	8,771,217 B2	7/2014	Lynch et al.
6,780,164 B2	8/2004	Bergheim et al.	8,801,648 B2	8/2014	Bergheim et al.
6,783,544 B2	8/2004	Lynch et al.	8,808,222 B2	8/2014	Schieber et al.
6,840,952 B2	1/2005	Saker et al.	8,827,990 B2	9/2014	Van Valen et al.
6,843,792 B2	1/2005	Nishtala et al.	8,852,137 B2	10/2014	Horvath et al.
6,893,415 B2	5/2005	Madsen et al.	8,876,898 B2	11/2014	Badawi et al.
6,955,656 B2	10/2005	Bergheim et al.	8,888,734 B2	11/2014	Nissan et al.
6,962,573 B1	11/2005	Wilcox	8,894,603 B2	11/2014	Badawi et al.
7,094,225 B2	8/2006	Tu et al.	8,926,546 B2	1/2015	Wilcox
7,135,009 B2	11/2006	Tu et al.	8,961,447 B2	2/2015	Schieber et al.
7,186,232 B1	3/2007	Smedley et al.	9,039,650 B2	5/2015	Schieber et al.
7,207,980 B2	4/2007	Christian et al.	9,044,301 B1	6/2015	Pinchuk et al.
7,273,475 B2	9/2007	Tu et al.	9,050,169 B2	6/2015	Schieber et al.
7,297,130 B2	11/2007	Bergheim et al.	9,066,750 B2	6/2015	Wardle et al.
7,331,984 B2	2/2008	Tu et al.	9,066,783 B2	6/2015	Euteneuer et al.
7,488,303 B1	2/2009	Haffner et al.	9,095,412 B2	8/2015	Badawi et al.
7,713,228 B2	5/2010	Robin	9,107,729 B2	8/2015	Sorensen et al.
7,740,604 B2	6/2010	Schieber et al.	9,125,723 B2	9/2015	Horvath et al.
7,806,847 B2	10/2010	Wilcox	9,155,655 B2	10/2015	Schieber et al.
7,850,637 B2	12/2010	Lynch et al.	9,192,516 B2	11/2015	Horvath et al.
7,867,205 B2	1/2011	Bergheim et al.	9,211,213 B2	12/2015	Wardle et al.
7,909,789 B2	3/2011	Badawi et al.	9,216,109 B2	12/2015	Badawi et al.
7,951,155 B2	5/2011	Smedley et al.	9,220,632 B2	12/2015	Smedley et al.
7,967,772 B2	6/2011	McKenzie et al.	9,226,850 B2	1/2016	Baerveldt et al.
			9,226,852 B2	1/2016	Schieber et al.
			9,301,875 B2	4/2016	Tu et al.
			9,326,891 B2	5/2016	Horvath et al.
			9,339,514 B2	5/2016	Bos et al.
			9,351,874 B2	5/2016	Schieber et al.
			9,358,155 B2	6/2016	Sorensen et al.
			9,358,156 B2	6/2016	Wardle et al.
			9,370,443 B2 *	6/2016	Badawi A61F 9/00781
			9,381,111 B2	7/2016	Hickingbotham et al.
			9,402,767 B2	8/2016	Schieber et al.
			9,486,361 B2 *	11/2016	Badawi A61F 9/00781
			9,492,319 B2	11/2016	Grieshaber et al.
			9,492,320 B2	11/2016	Lynch et al.
			9,510,973 B2	12/2016	Wardle
			9,855,167 B2	1/2018	Badawi et al.
			9,895,258 B2	2/2018	Badawi et al.
			2001/0014788 A1	8/2001	Morris
			2002/0013546 A1	1/2002	Grieshaber et al.

US 10,314,742 B2

Page 3

(56)

References Cited

U.S. PATENT DOCUMENTS

2002/0013572	A1	1/2002	Berlin	2011/0224597	A1	9/2011	Stegmann et al.
2002/0055753	A1	5/2002	Silvestrini	2011/0238009	A1	9/2011	Meron et al.
2002/0072673	A1	6/2002	Yamamoto et al.	2011/0238075	A1	9/2011	Clauson et al.
2002/0133168	A1	9/2002	Smedley et al.	2011/0306915	A1	12/2011	De Juan, Jr. et al.
2002/0143284	A1	10/2002	Tu et al.	2012/0010702	A1	1/2012	Stegmann et al.
2003/0060447	A1	3/2003	Karakelle et al.	2012/0123315	A1	5/2012	Horvath et al.
2003/0060873	A1	3/2003	Gertner et al.	2012/0123434	A1	5/2012	Grabner et al.
2003/0120200	A1	6/2003	Bergheim et al.	2012/0136306	A1	5/2012	Bartha
2003/0181848	A1	9/2003	Bergheim et al.	2012/0165720	A1	6/2012	Horvath et al.
2003/0229303	A1	12/2003	Haffner et al.	2012/0191064	A1	7/2012	Conston et al.
2003/0236483	A1	12/2003	Ren	2012/0197175	A1	8/2012	Horvath et al.
2003/0236484	A1	12/2003	Lynch et al.	2012/0203160	A1	8/2012	Kahook et al.
2004/0044310	A1	3/2004	Suzuki	2012/0220917	A1	8/2012	Silvestrini et al.
2004/0193095	A1	9/2004	Shadduck	2012/0310072	A1	12/2012	Grieshaber
2004/0193262	A1	9/2004	Shadduck	2012/0310137	A1	12/2012	Silvestrini
2004/0210181	A1	10/2004	Vass et al.	2013/0041346	A1	2/2013	Alon
2004/0254519	A1	12/2004	Tu et al.	2013/0158462	A1	6/2013	Wardle et al.
2004/0254520	A1	12/2004	Porteous et al.	2013/0245600	A1	9/2013	Yamamoto et al.
2004/0254521	A1	12/2004	Simon	2013/0253402	A1	9/2013	Badawi et al.
2004/0260228	A1	12/2004	Lynch et al.	2013/0274655	A1	10/2013	Jennings et al.
2005/0055082	A1	3/2005	Ben Muvhar et al.	2014/0066833	A1	3/2014	Yaron et al.
2005/0101967	A1	5/2005	Weber et al.	2014/0081194	A1	3/2014	Burns et al.
2005/0171507	A1	8/2005	Christian	2014/0121584	A1	5/2014	Wardle et al.
2005/0192527	A1	9/2005	Gharib et al.	2014/0128847	A1	5/2014	Lopez
2005/0209549	A1	9/2005	Bergheim et al.	2014/0135916	A1	5/2014	Clauson et al.
2005/0250788	A1	11/2005	Tu et al.	2014/0163448	A1	6/2014	Lind et al.
2005/0266047	A1	12/2005	Tu et al.	2014/0171852	A1	6/2014	Khor
2005/0267555	A1	12/2005	Marnfeldt et al.	2014/0194916	A1	7/2014	Ichikawa
2005/0277864	A1	12/2005	Haffner et al.	2014/0213958	A1	7/2014	Clauson et al.
2005/0288619	A1	12/2005	Gharib et al.	2014/0236066	A1	8/2014	Horvath et al.
2006/0032507	A1	2/2006	Tu	2014/0276332	A1	9/2014	Crimaldi et al.
2006/0036207	A1	2/2006	Koonmen et al.	2014/0288485	A1	9/2014	Berlin
2006/0069340	A1	3/2006	Simon	2014/0309599	A1	10/2014	Schaller
2006/0074375	A1	4/2006	Bergheim et al.	2014/0364791	A1	12/2014	Stegmann et al.
2006/0084907	A1	4/2006	Bergheim et al.	2015/0005623	A1	1/2015	Grover et al.
2006/0149194	A1	7/2006	Conston	2015/0011926	A1	1/2015	Reitsamer et al.
2006/0155300	A1	7/2006	Stamper et al.	2015/0051699	A1	2/2015	Badawi et al.
2006/0173077	A1	8/2006	Cagle	2015/0065940	A1	3/2015	Rangel-Friedman et al.
2006/0173397	A1	8/2006	Tu et al.	2015/0073328	A1	3/2015	Badawi et al.
2006/0173446	A1	8/2006	Dacquay et al.	2015/0080783	A1	3/2015	Berlin
2006/0195055	A1	8/2006	Bergheim et al.	2015/0112372	A1	4/2015	Perez Grossmann
2006/0195056	A1	8/2006	Bergheim et al.	2015/0119787	A1	4/2015	Wardle et al.
2006/0195187	A1	8/2006	Stegmann et al.	2015/0125328	A1	5/2015	Bourne et al.
2006/0200113	A1	9/2006	Haffner et al.	2015/0133946	A1	5/2015	Horvath et al.
2006/0217741	A1	9/2006	Ghannoum	2015/0148615	A1	5/2015	Brennan et al.
2006/0241580	A1	10/2006	Mittelstein et al.	2015/0216729	A1	8/2015	Doci
2007/0073275	A1	3/2007	Conston et al.	2015/0223981	A1	8/2015	Smedley et al.
2007/0106236	A1	5/2007	Coroneo	2015/0223983	A1	8/2015	Schieber et al.
2007/0191863	A1	8/2007	De Juan, Jr. et al.	2015/0250649	A1	9/2015	Euteneuer et al.
2007/0260173	A1	11/2007	Boukhny et al.	2015/0257932	A1	9/2015	Pinchuk et al.
2007/0276420	A1	11/2007	Sorensen et al.	2015/0282982	A1	10/2015	Schieber et al.
2008/0004596	A1	1/2008	Yun et al.	2015/0313758	A1	11/2015	Wilcox
2008/0058704	A1	3/2008	Hee et al.	2015/0320596	A1	11/2015	Gifford, III et al.
2008/0058760	A1	3/2008	Agerup	2015/0335481	A1	11/2015	Badawi et al.
2008/0082078	A1	4/2008	Berlin	2015/0374545	A1	12/2015	Horvath et al.
2008/0300574	A1	12/2008	Belson et al.	2016/0022486	A1	1/2016	Clauson et al.
2009/0036819	A1	2/2009	Tu et al.	2016/0051408	A1	2/2016	Baerveldt et al.
2009/0043321	A1	2/2009	Conston et al.	2016/0095985	A1	4/2016	Novak
2009/0082862	A1	3/2009	Schieber et al.	2016/0100980	A1	4/2016	Badawi et al.
2009/0132040	A1	5/2009	Frion et al.	2016/0106589	A1	4/2016	Mittelstein et al.
2009/0227934	A1	9/2009	Euteneuer et al.	2016/0135994	A1	5/2016	Romoda et al.
2009/0247955	A1	10/2009	Yamamoto et al.	2016/0143778	A1	5/2016	Aljuri et al.
2009/0287143	A1	11/2009	Line	2016/0151204	A1	6/2016	Haffner et al.
2009/0287233	A1	11/2009	Huculak	2016/0220417	A1	8/2016	Schieber et al.
2010/0019177	A1	1/2010	Luckevich	2016/0220418	A1	8/2016	Sorensen et al.
2010/0087774	A1	4/2010	Haffner et al.	2016/0256317	A1	9/2016	Horvath et al.
2010/0121248	A1	5/2010	Yu et al.	2016/0256323	A1	9/2016	Horvath et al.
2010/0173866	A1	7/2010	Hee et al.	2016/0287438	A1	10/2016	Badawi et al.
2010/0179652	A1	7/2010	Yamamoto et al.	2016/0302965	A1	10/2016	Erickson et al.
2010/0222802	A1	9/2010	Gillespie	2016/0331588	A1	11/2016	Ambati et al.
2010/0241046	A1	9/2010	Pinchuk et al.	2016/0346006	A1	12/2016	Hickengbotham et al.
2010/0262174	A1	10/2010	Sretavan et al.	2016/0354248	A1	12/2016	Kahook
2011/0009874	A1	1/2011	Wardle et al.	2017/0143541	A1	5/2017	Badawi et al.
2011/0009958	A1	1/2011	Wardle et al.	2017/0202707	A1	7/2017	Badawi et al.
2011/0098809	A1	4/2011	Wardle et al.	2017/0258507	A1	9/2017	Hetherington
				2017/0348152	A1	12/2017	Badawi et al.
				2018/0271699	A1	9/2018	Badawi et al.

US 10,314,742 B2

Page 4

(56)

References Cited

U.S. PATENT DOCUMENTS

FOREIGN PATENT DOCUMENTS

JP	2005-510317	A	4/2005
JP	2005-538809	A	12/2005
WO	WO-00/64393	A1	11/2000
WO	WO-03/045582	A1	6/2003
WO	WO-2004/026361	A1	4/2004
WO	WO-2005/105197	A2	11/2005
WO	WO-2005/105197	A3	11/2005
WO	WO-2005/107664	A2	11/2005
WO	WO-2005/107664	A3	11/2005
WO	WO-2005/117752	A1	12/2005
WO	WO-2006/066103	A2	6/2006
WO	WO-2006/066103	A3	6/2006
WO	WO-2008/002377	A1	1/2008
WO	WO-2009/042596	A2	4/2009
WO	WO-2009/042596	A3	4/2009
WO	WO-2011/097408	A1	8/2011
WO	WO-2011/106781	A1	9/2011
WO	WO-2013/141898	A1	9/2013
WO	WO-2016/042162	A1	3/2016
WO	WO-2016/159999	A1	10/2016

OTHER PUBLICATIONS

Extended European Search Report dated Apr. 22, 2015, for EP Patent Application No. 11 740 372.5, filed Feb. 3, 2011, 6 pages.

Extended European Search Report dated Jun. 9, 2016, for European Patent Application No. 16 155 079.3, filed on May 31, 2007, 7 pages.

Extended European Search Report dated May 17, 2011, for European Patent Application No. 11 162 487.0, filed on May 31, 2007, 6 pages.

Extended European Search Report dated Mar. 24, 2016, for European Patent Application No. 12 871 982.0, filed on Oct. 4, 2012, 7 pages.

Final Office Action dated Nov. 1, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 12 pages.

Final Office Action dated Jul. 19, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 6 pages.

Final Office Action dated Feb. 1, 2013, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 6 pages.

Final Office Action dated Sep. 15, 2014, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 13 pages.

Final Office Action dated Sep. 20, 2013, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 16 pages.

Final Office Action dated Nov. 12, 2013, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 8 pages.

Final Office Action dated Jan. 8, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 8 pages.

Final Office Action dated Sep. 3, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 8 pages.

Final Office Action dated Apr. 23, 2015, for U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 8 pages.

Final Office Action dated Aug. 19, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 6 pages.

Final Office Action dated Mar. 9, 2016, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 11 pages.

Final Office Action dated Oct. 3, 2016, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 27 pages.

International Search Report dated Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, 4 pages.

International Search Report dated Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 2 pages.

International Search Report dated Feb. 1, 2013 for PCT Application No. PCT/US2012/058751, filed on Oct. 4, 2012, 4 pages.

International Search Report dated Sep. 14, 2015, for PCT Application No. PCT/US2015/023720, filed on Mar. 31, 2015, 5 pages.

Non-Final Office Action dated May 17, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 10 pages.

Non-Final Office Action dated Jan. 26, 2012, for U.S. Appl. No. 12/695,053, filed Jan. 27, 2010, 10 pages.

Non-Final Office Action dated Mar. 15, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 4 pages.

Non-Final Office Action dated May 11, 2012, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 5 pages.

Non-Final Office Action dated Nov. 9, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 5 pages.

Non-Final Office Action dated Apr. 24, 2013, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 13 pages.

Non-Final Office Action dated Jun. 12, 2013, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 8 pages.

Non-Final Office Action dated Sep. 9, 2013, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.

Non-Final Office Action dated Feb. 7, 2014, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 12 pages.

Non-Final Office Action dated Feb. 24, 2014, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 12 pages.

Non-Final Office Action dated May 15, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.

Non-Final Office Action dated Nov. 28, 2014, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 7 pages.

Non-Final Office Action dated Jan. 14, 2015, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 10 pages.

Non-Final Office Action dated Feb. 4, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 6 pages.

Non-Final Office Action dated Feb. 23, 2015, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 17 pages.

Non-Final Office Action dated Jul. 10, 2015, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 16 pages.

Non-Final Office Action dated Oct. 7, 2015, for U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 5 pages.

Non-Final Office Action dated Nov. 3, 2015, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 7 pages.

Non-Final Office Action dated Dec. 14, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 7 pages.

Non-Final Office Action dated Jun. 7, 2016, for U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 5 pages.

Non-Final Office Action dated Feb. 25, 2016, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 19 pages.

Notice of Allowance dated Feb. 2, 2011, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 6 pages.

Notice of Allowance dated Jun. 11, 2012, for U.S. Appl. No. 12/695,053, filed Jan. 27, 2010, 7 pages.

Notice of Allowance dated Apr. 2, 2013, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 6 pages.

Notice of Allowance dated May 10, 2013, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 8 pages.

Notice of Allowance dated Jul. 7, 2014, for U.S. Appl. No. 14/012,963, filed Aug. 28, 2013, 6 pages.

Notice of Allowance dated Jul. 23, 2014, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 8 pages.

Notice of Allowance dated Mar. 30, 2015, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 5 pages.

Notice of Allowance dated Aug. 10, 2015, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.

Notice of Allowance dated Mar. 1, 2016, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 7 pages.

Corrected Notice of Allowability dated Apr. 25, 2016, U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 2 pages.

Notice of Allowance dated Jul. 13, 2016, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 7 pages.

Corrected Notice of Allowability dated Sep. 1, 2016, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 2 pages.

Written Opinion dated Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, 6 pages.

Written Opinion dated Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 5 pages.

Written Opinion dated Feb. 1, 2013 for PCT Application No. PCT/US2012/058751, filed on Oct. 4, 2012, 6 pages.

Written Opinion dated Sep. 14, 2015 for PCT Application No. PCT/US15/23720, filed on Mar. 31, 2015, 8 pages.

U.S. Appl. No. 15/343,147, filed Nov. 3, 2016, by Badawi et al.

US 10,314,742 B2

Page 5

(56)

References Cited

OTHER PUBLICATIONS

U.S. Appl. No. 15/340,911, filed Nov. 1, 2016, by Badawi et al.
Corrected Notice of Allowability dated Nov. 23, 2018, for U.S. Appl. No. 14/816,822, filed Aug. 3, 2015, 2 pages.
Final Office Action dated May 18, 2017, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 14 pages.
Final Office Action dated Jan. 29, 2018, for U.S. Appl. No. 14/973,620, filed Dec. 17, 2015, 19 pages.
Final Office Action dated Apr. 6, 2018, for U.S. Appl. No. 15/683,652, filed Aug. 22, 2017, 11 pages.
Final Office Action dated Jun. 1, 2018, for U.S. Appl. No. 14/816,822, filed Aug. 3, 2015, 6 pages.
Final Office Action dated Oct. 19, 2018, for U.S. Appl. No. 15/683,652, filed Aug. 22, 2017, 8 pages.
Non-Final Office Action dated Jan. 18, 2017, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 13 pages.
Non-Final Office Action dated Mar. 22, 2017, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 31 pages.

Non-Final Office Action dated Aug. 28, 2017, for U.S. Appl. No. 14/973,620, filed Dec. 17, 2015, 6 pages.
Non-Final Office Action dated Nov. 7, 2017, for U.S. Appl. No. 14/816,822, filed Aug. 3, 2015, 14 pages.
Non-Final Office Action dated Dec. 15, 2017, for U.S. Appl. No. 15/343,147, filed Nov. 3, 2016, 12 pages.
Non-Final Office Action dated Apr. 4, 2018, for U.S. Appl. No. 14/675,580, filed Mar. 31, 2015, 10 pages.
Non-Final Office Action dated Aug. 29, 2018, for U.S. Appl. No. 14/973,620, filed Dec. 17, 2015, 11 pages.
Non-Final Office Action dated Sep. 20, 2018, for U.S. Appl. No. 15/340,911, filed Nov. 1, 2016, 7 pages.
Notice of Allowance dated Oct. 25, 2017, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 8 pages.
Notice of Allowance dated Nov. 21, 2017, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 10 pages.
Notice of Allowance dated Aug. 31, 2018, for U.S. Appl. No. 14/816,822, filed Aug. 3, 2015, 7 pages.

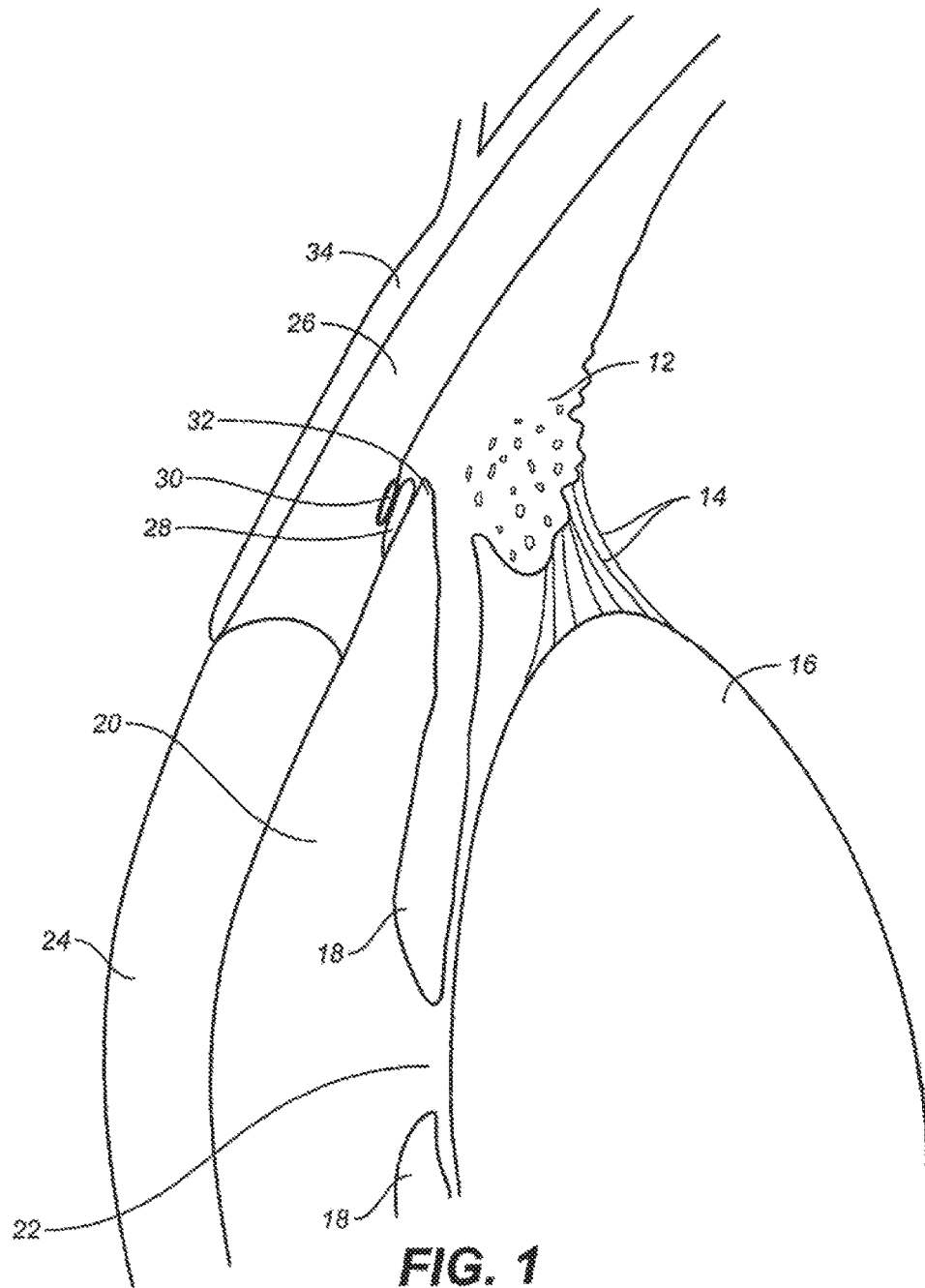
* cited by examiner

U.S. Patent

Jun. 11, 2019

Sheet 1 of 16

US 10,314,742 B2



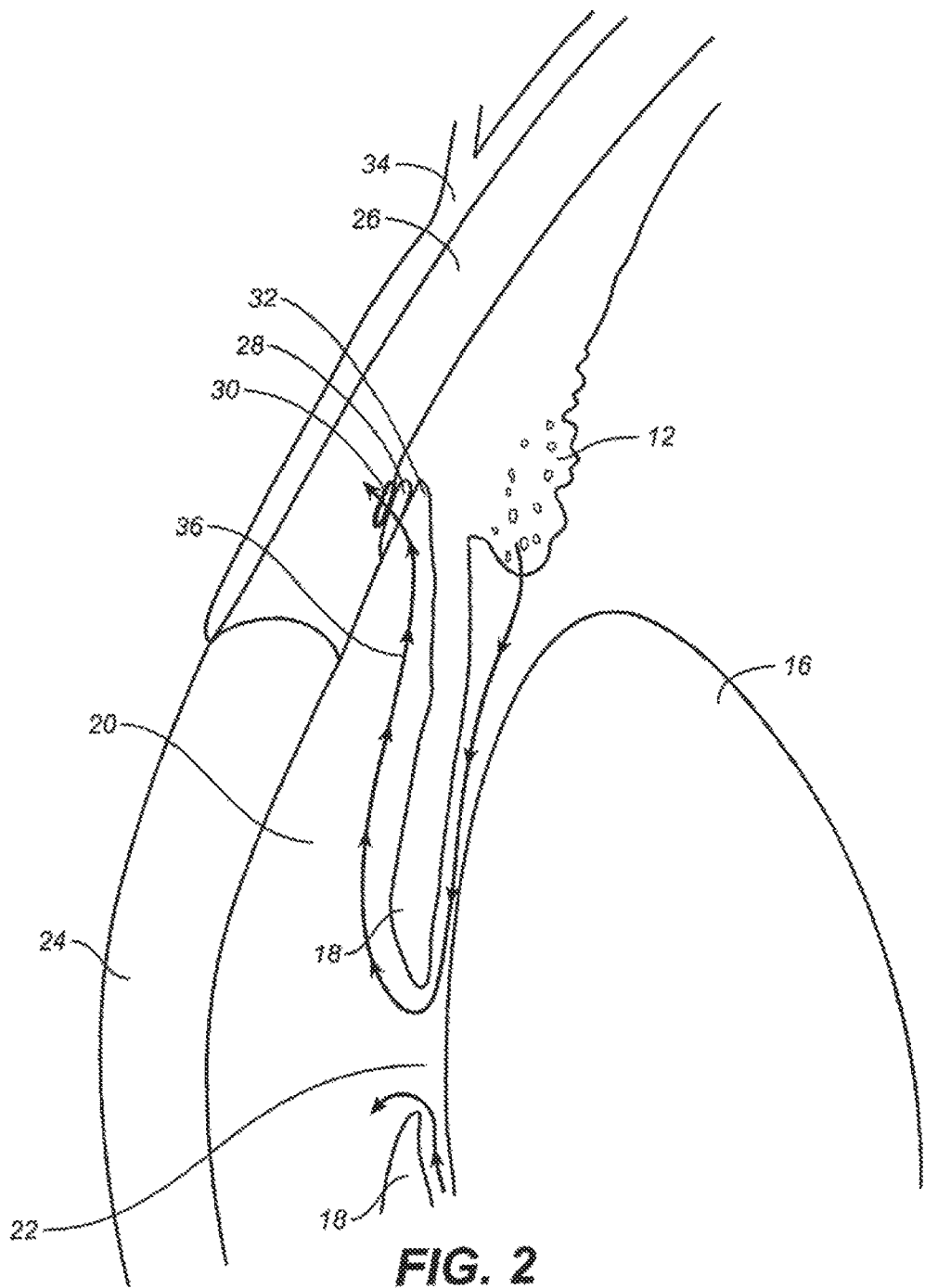


FIG. 2

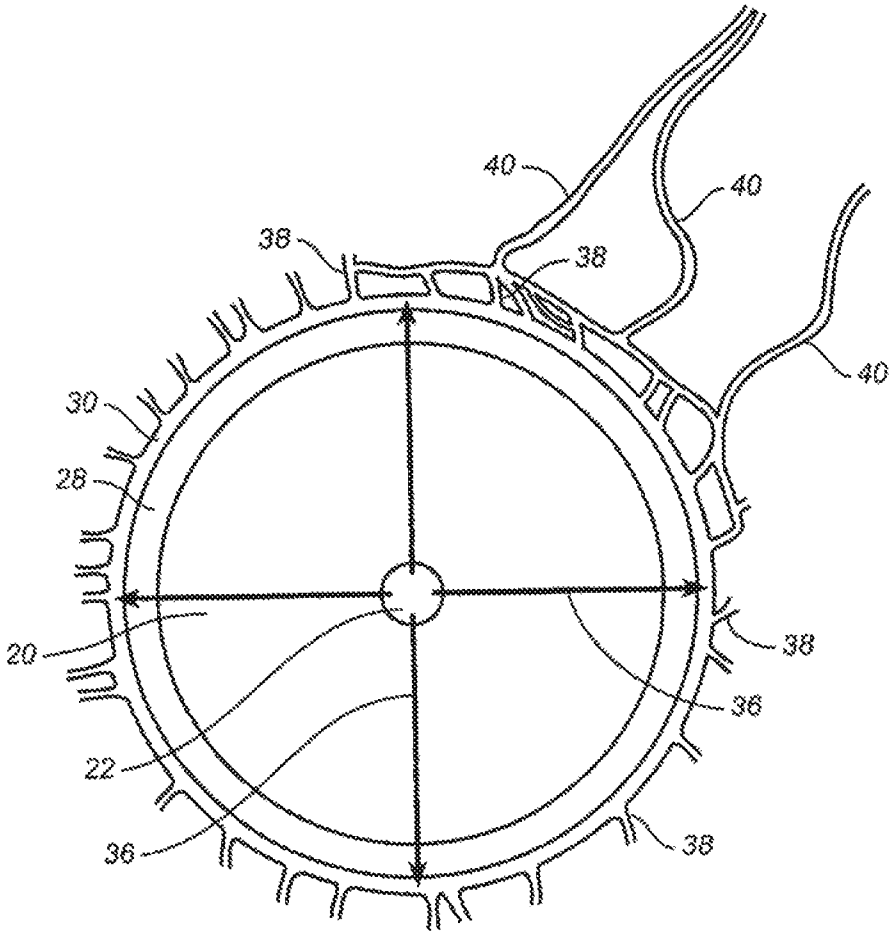


FIG. 3

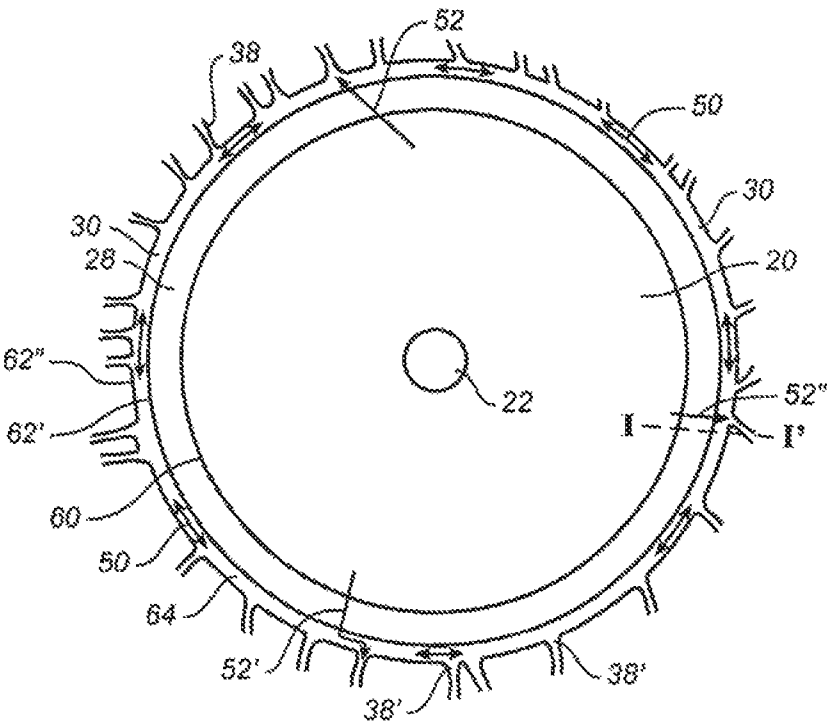


FIG. 4A

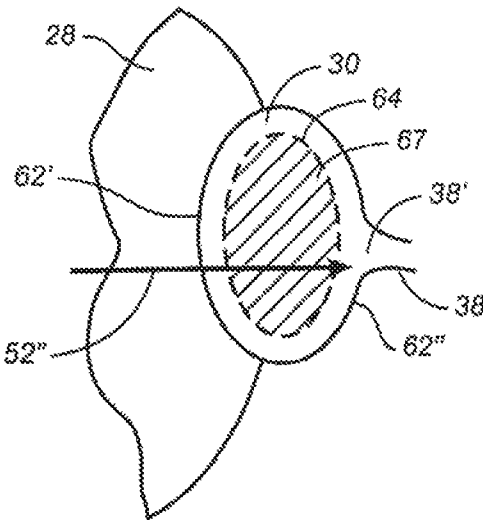
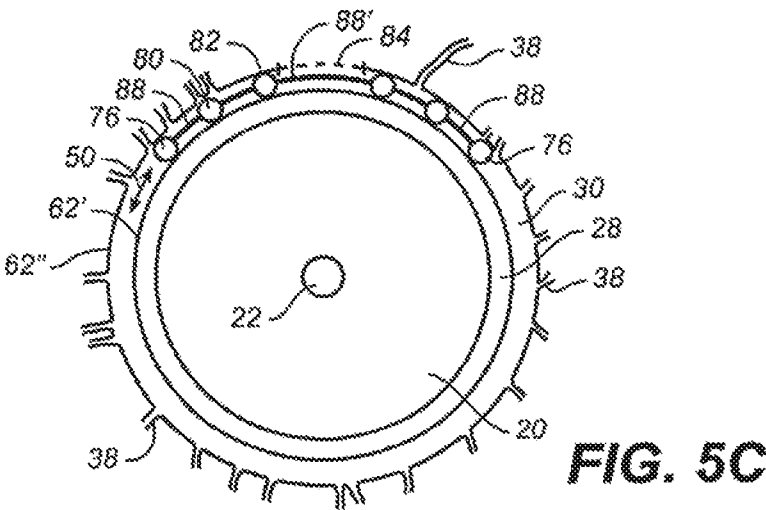
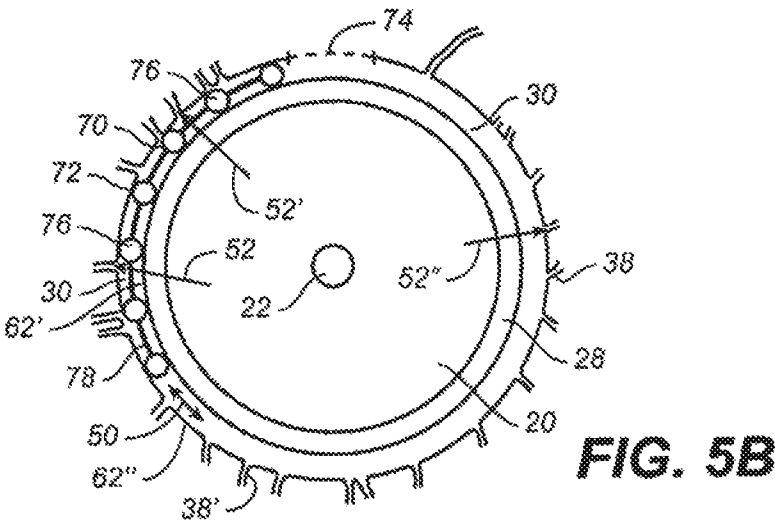
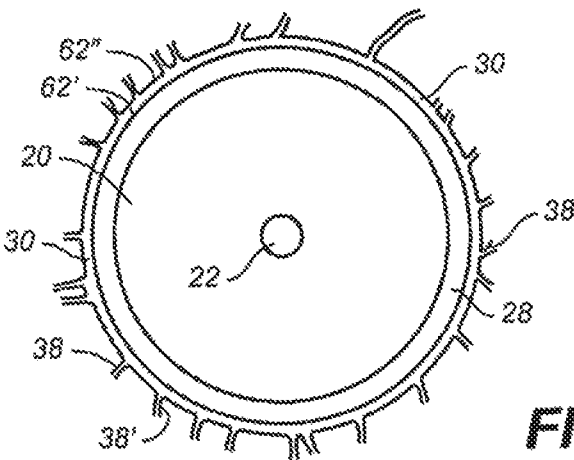


FIG. 4B



U.S. Patent

Jun. 11, 2019

Sheet 6 of 16

US 10,314,742 B2

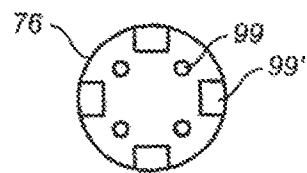
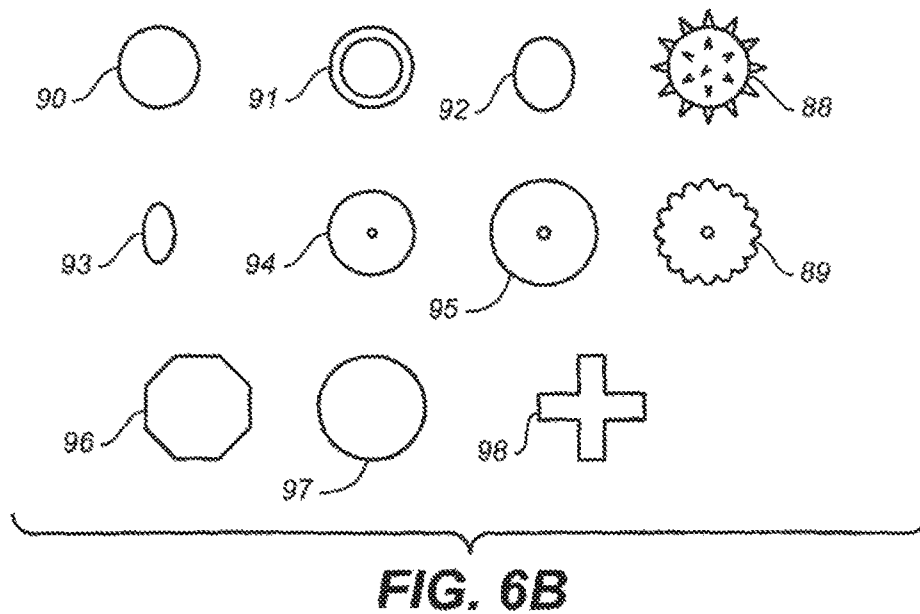
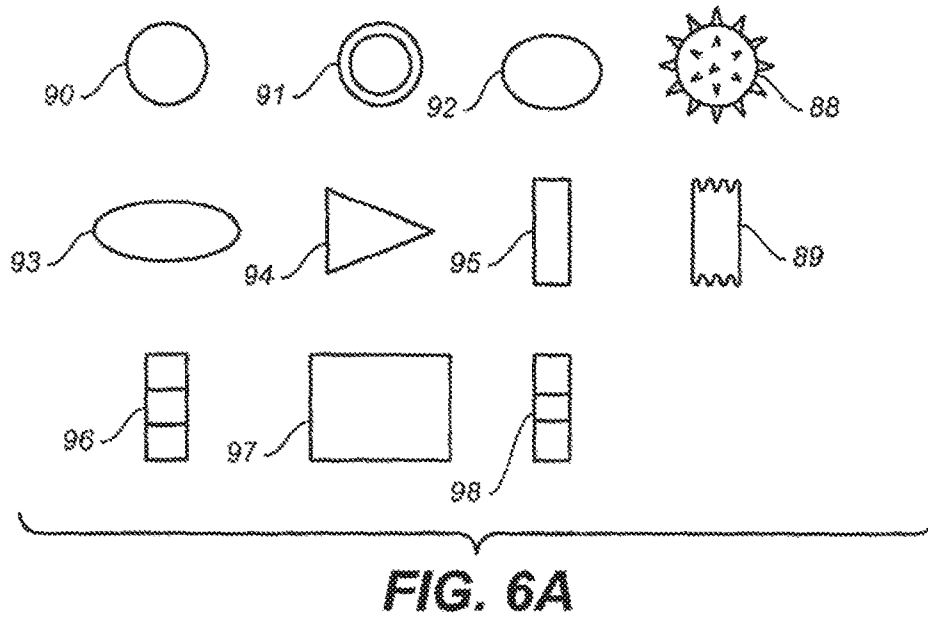




FIG. 7A



FIG. 7B

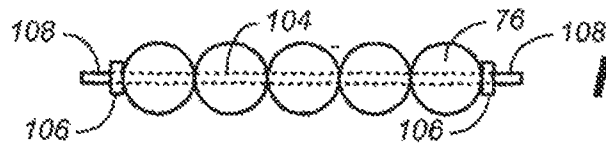


FIG. 7C

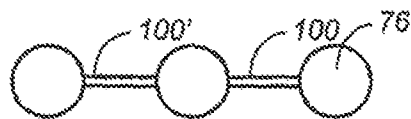


FIG. 7D

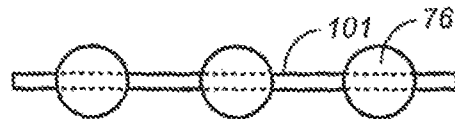


FIG. 7E

U.S. Patent

Jun. 11, 2019

Sheet 8 of 16

US 10,314,742 B2

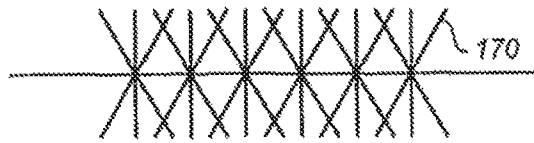


FIG. 8A

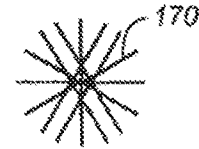


FIG. 8B

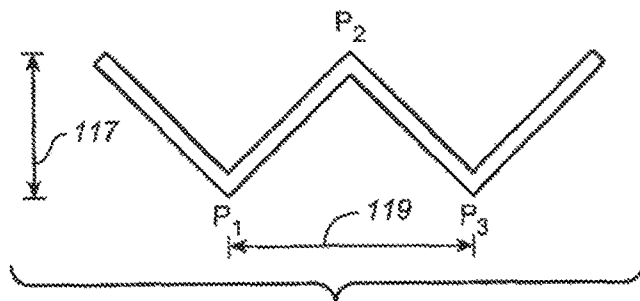


FIG. 8C



FIG. 8D

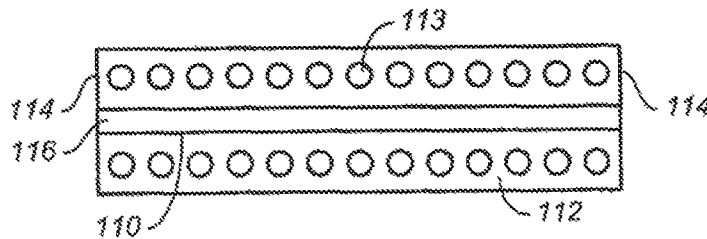


FIG. 8E

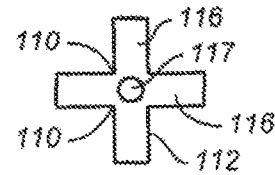


FIG. 8F

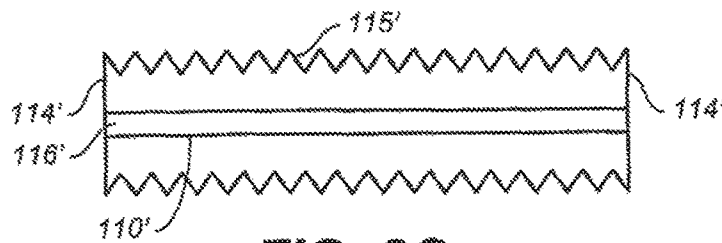


FIG. 8G

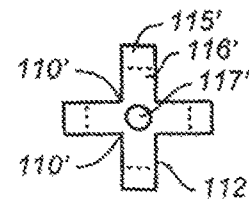


FIG. 8H

U.S. Patent

Jun. 11, 2019

Sheet 9 of 16

US 10,314,742 B2

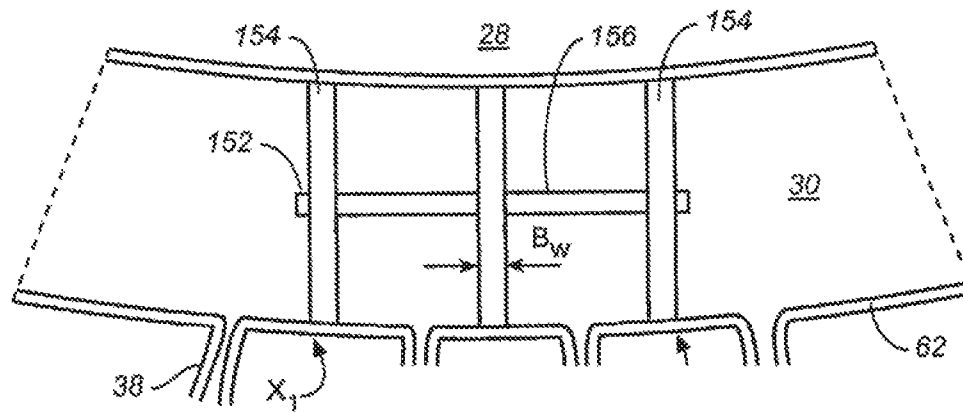


FIG. 9A

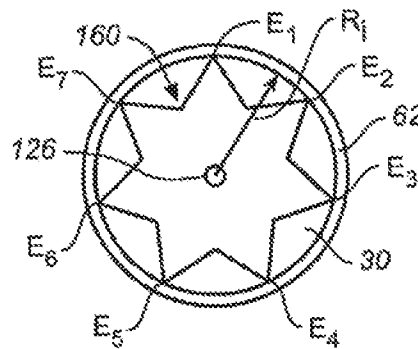


FIG. 9B

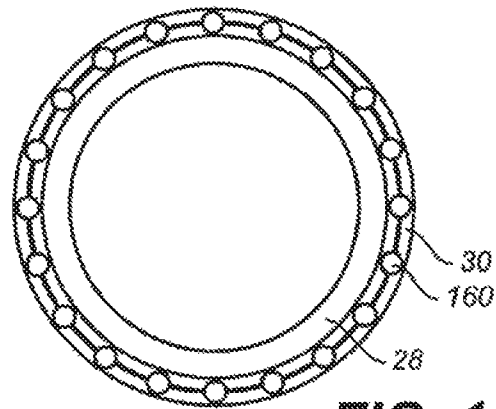


FIG. 10A

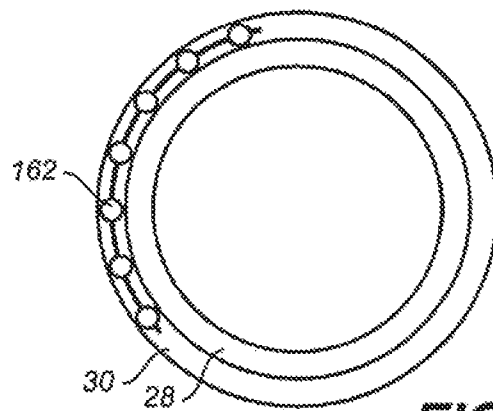


FIG. 10B

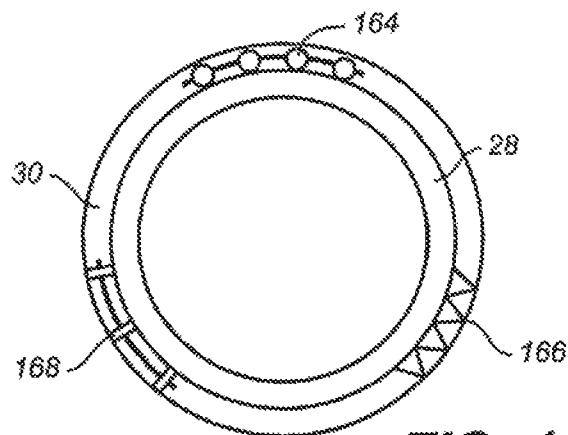


FIG. 10C

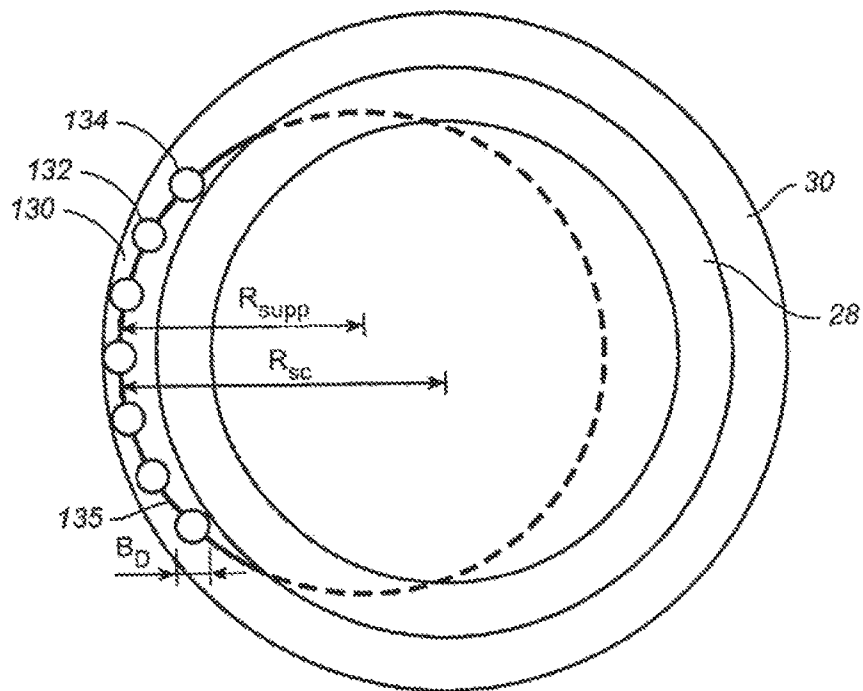


FIG. 11A

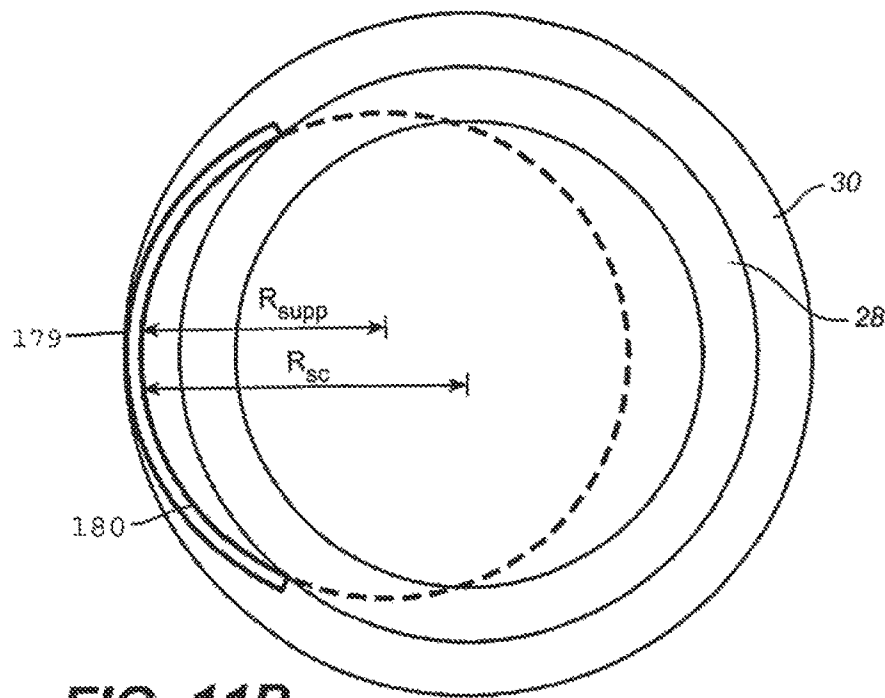


FIG. 11B

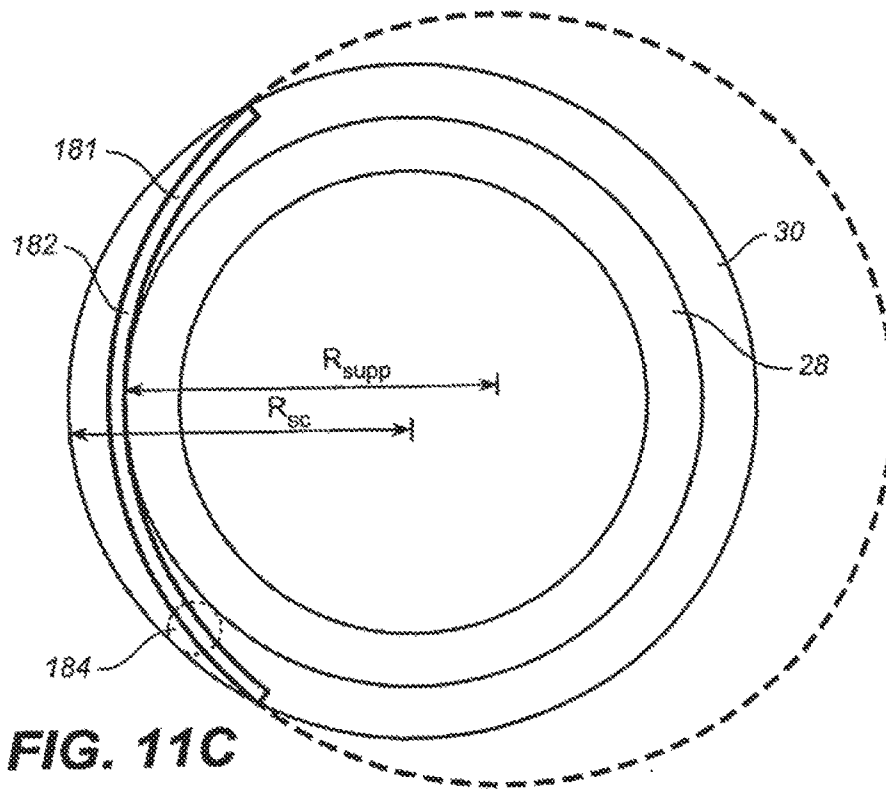


FIG. 11C

U.S. Patent

Jun. 11, 2019

Sheet 13 of 16

US 10,314,742 B2

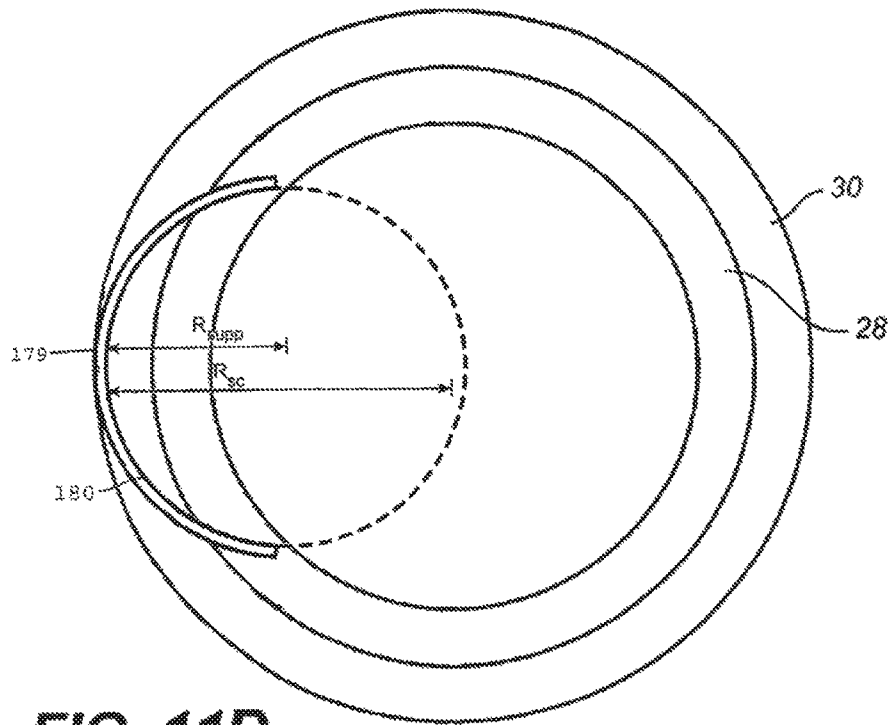


FIG. 11D

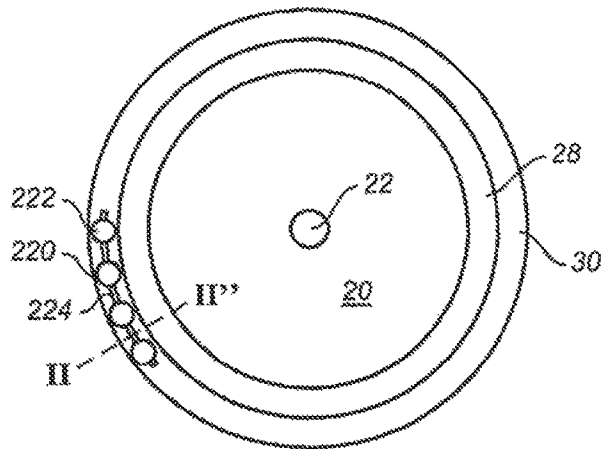


FIG. 12A

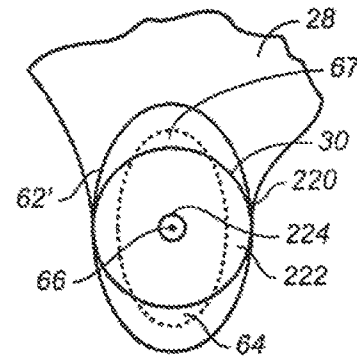


FIG. 12B

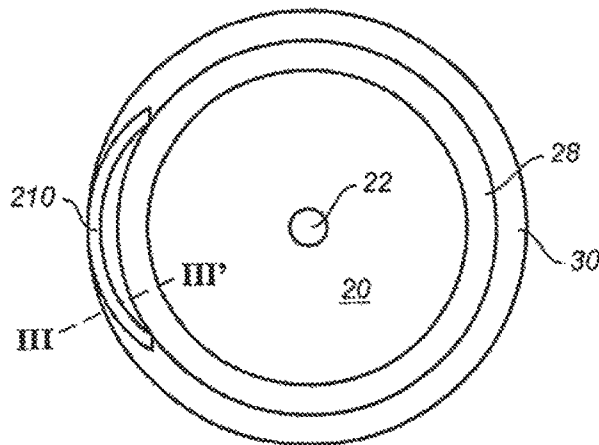


FIG. 12C

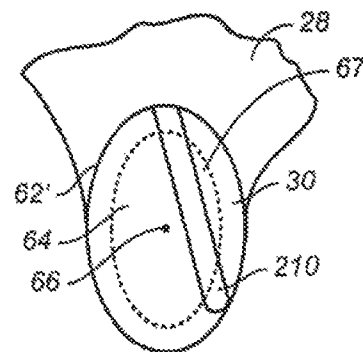


FIG. 12D

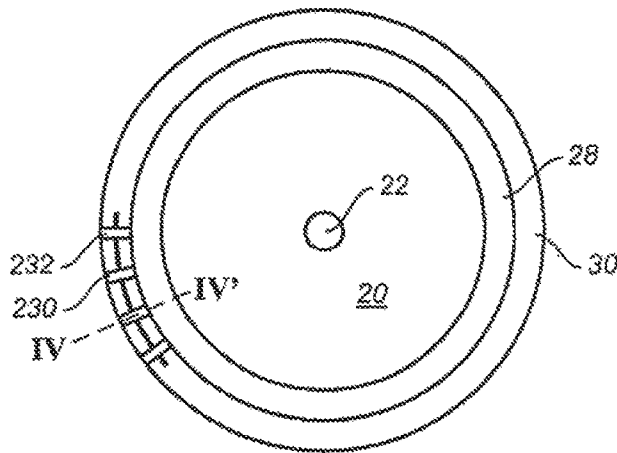


FIG. 12E

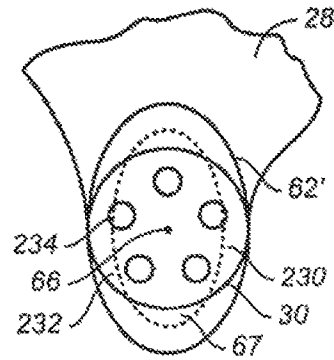


FIG. 12F

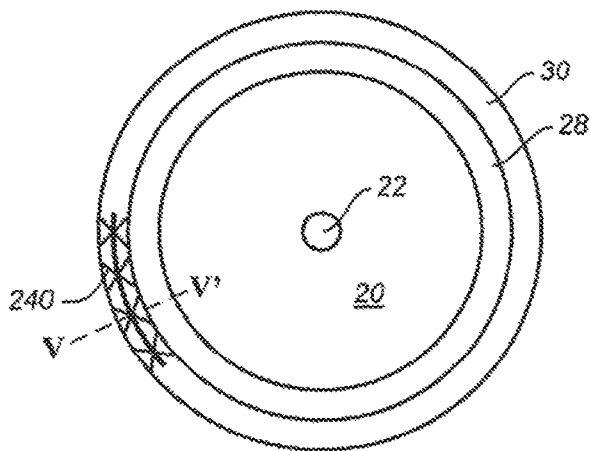


FIG. 12G

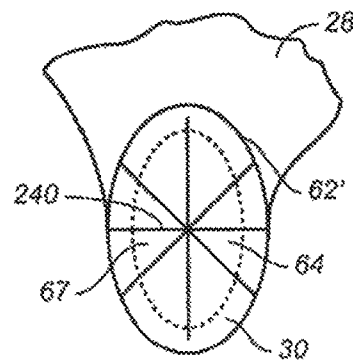


FIG. 12H

U.S. Patent

Jun. 11, 2019

Sheet 16 of 16

US 10,314,742 B2

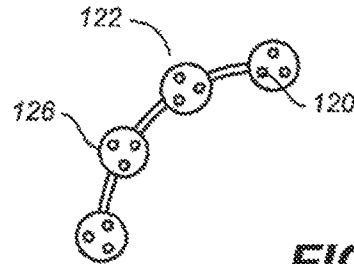


FIG. 13

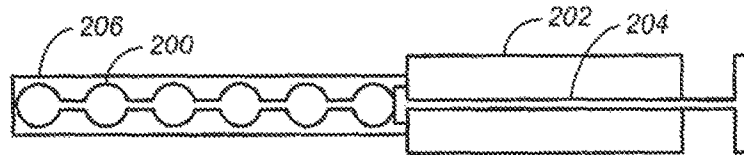


FIG. 14A

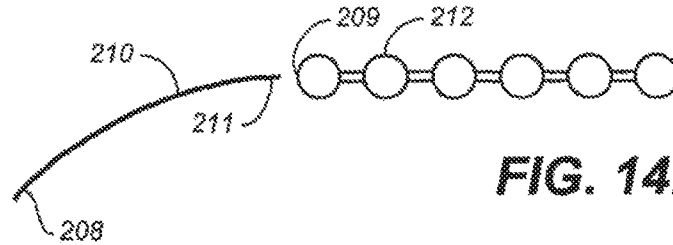


FIG. 14B



FIG. 14C

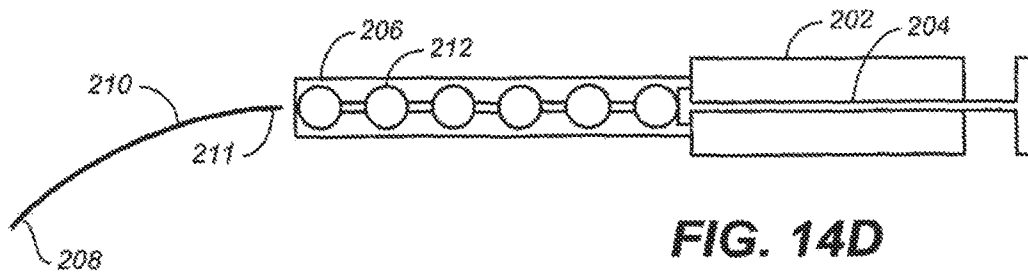


FIG. 14D

US 10,314,742 B2

1

**INTRAOCULAR IMPLANTS AND METHODS
AND KITS THEREFOR****CROSS-REFERENCE TO RELATED
APPLICATIONS**

This application is a continuation of U.S. patent application Ser. No. 13/025,112, filed Feb. 10, 2011, now issued as U.S. Pat. No. 9,370,443, which is a divisional of U.S. patent application Ser. No. 11/475,523, filed Jun. 26, 2006, now issued as U.S. Pat. No. 7,909,789, each of which is hereby incorporated by reference in its entirety.

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical

2

therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjunctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmural flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal. The support does not substantially interfere with transmural flow across Schlemm's canal, and thereby uti-

US 10,314,742 B2

3

lizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocompatible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer; a polyorthoester; a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a poly-anhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, cubical, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted between three beads, the connectors may be of the same or different lengths. The connectors can include the same or

4

different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmurial flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can include implanting at least two supports. If more than one support is implanted within a single eye, the multiple

US 10,314,742 B2

5

supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 provides a partial cross-sectional side view of a normal human eye.

FIG. 2 provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. 3 shows a front view of normal fluid drainage from the eye.

FIG. 4A shows an alternative front view of normal fluid drainage paths from the eye. FIG. 4B shows a cross-sectional view along line I-I'.

FIG. 5A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. 5B shows a front view of a device including a support inserted into Schlemm's canal that allows transmural flow across the canal. FIG. 5C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmural flow across the canal.

FIG. 6A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. 6B shows the corresponding front views of the element or bead configurations shown in FIG. 6A. FIG. 6C illustrates an element or bead having fenestrations.

FIG. 7A illustrates a support having multiple juxtaposed beads. FIG. 7B illustrates a support having multiple juxtaposed and connected beads. FIG. 7C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. 7D shows a support having multiple, spaced-apart but connected beads. FIG. 7E illustrates beads threaded onto a connector.

FIGS. 8A-B show side and front views, respectively, of a support having an open network structure. FIGS. 8C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at at least three points (labeled P₁, P₂, P₃). FIGS. 8E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. 8G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. 9A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. 10A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. 11A-B and D illustrate configurations of supports having a smaller radius of curvature than Schlemm's canal. FIG. 11C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. 12A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. 12B shows a cross-sectional view along line II-II'. FIG. 12C illustrates a variation of a support traversing the central core

6

of the canal. FIG. 12D shows a cross-sectional view along line III-III'. FIG. 12E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. 12F shows a cross-sectional view along line IV-IV'. FIG. 12G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. 12H shows a cross-sectional view along line V-V'.

FIG. 13 shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. 14A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. 14B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. 14C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. 14D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmural fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. 1 shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body 12 is connected to iris 18 and to lens 16 via zonular fibrils 14. The anterior chamber of the eye 20 is bounded on its anterior (front) surface by cornea 24. In the center of iris 18 is pupil 22. Cornea 24 is connected on its periphery to sclera 26, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork 28 is located on the outer peripheral surface of anterior chamber 20. The trabecular meshwork extends 360° circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork 28 is Schlemm's canal 30. Schlemm's canal extends 360° circumferentially around the trabecular meshwork. At the apex formed between iris 18, meshwork 28 and sclera 26 is angle 32. Conjunctiva 34 is a membrane overlaying sclera 26 and lining the inside of the eyelid (not shown).

FIG. 2 shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body 12 and its path through and out of the eye is indicated by solid directional line 36. The aqueous humor flows from ciliary body 12, between lens 16 and iris 18, through pupil 22 into anterior chamber 20, across trabecular meshwork 28, across Schlemm's canal 30, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. 3 shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber 20 via pupil 22. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines 36. The fluid crosses trabecular meshwork 28 and traverses Schlemm's canal 30 to reach aqueous veins or collector channels 38. There are typically 25-30 collector channels located in a human eye. Collector channels 38 are connected to vasculature 40, whereby the drained aqueous humor enters the bloodstream. Although

US 10,314,742 B2

7

the direction of net or bulk fluid flow is depicted as radially outward by directional lines 36 from pupil 22 for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. 4A-B. FIG. 4A shows a front view of an eye, and FIG. 4B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal 30 is depicted by directional lines 50. Fluid that does not traverse canal 30 to reach collector channels 38 may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines 52, 52', and 52". In each of these paths, fluid enters trabecular meshwork 28 along its inner peripheral surface 60 and exits the meshwork along its outer peripheral surface 62'. Meshwork outer peripheral surface 62' provides the inner peripheral surface or wall of Schlemm's canal 30. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork 38 through inner peripheral surface or wall 62' of Schlemm's canal 30 to reach lumen 64 of the canal. Second, fluid must flow from lumen 64 through canal outer peripheral wall 62" through apertures 38' to enter collector channels 38. Finally, the collector channels 38 feed the drained fluid into vasculature. Lumen 64 of canal 30 includes a central core region 67. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflow from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1) fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral bound-

8

ary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the connector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. 5A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal 30, where canal outer peripheral wall 62" is very close to canal inner peripheral wall 62'. Although Schlemm's canal 30 is depicted in FIG. 5A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels 38 is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. 5B illustrates an example of a device 70 inserted into Schlemm's canal 30 through incision site 74. Device 70 in this example is positioned to one side of incision site 74. Device 70 includes support 72 that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall 62' and canal outer wall 62" to reach collector channels 38 via apertures 38'. In the example shown in FIG. 5B, support 72 includes elements or beads 76 connected with connectors 78. In this variation, the distance between canal inner wall 62' and outer wall 62" is approximately determined by the cross-sectional dimension of support 72, which is in turn determined by the largest cross-sectional diameter of the beads 76. Therefore, circumferential (i.e., longitudinal) fluid flow around and along the canal 30 indicated by directional line 50 may be inhibited by

US 10,314,742 B2

9

the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52''** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters (e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. 5C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. 5B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. 6A and 6B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges, **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. 6C, elements or beads **76** may include fenestrations **99**, **99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. 6C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. 7A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. 7A), connected and juxtaposed (FIGS. 7B and 7C), or connected together with connectors **100**, **100'** to form intervals between beads (FIG. 7D). In addition, beads may be threaded onto a connector **101** (FIG. 7E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. 7B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. 7C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knot-

10

ting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. 7D, multiple connectors **100**, **100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100**, **100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100**, **100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. 7E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100**, **100'**, **101** can be flexible, such as thin polymer threads or metal wires. Connectors **100**, **100'**, **101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100**, **100'**, **101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. 8A-F. As illustrated in FIG. 8A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. 8A-B will have minimal surface area contact with the walls of Schlemm's canal, i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. 8C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. 8C, the support will contact the wall of Schlemm's canal at at least three points, labeled P_1 , P_2 , and P_3 , after implantation. In FIGS. 8E-H, examples of rod-like supports having fluted edges are shown. In FIGS. 8E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include fenestrations **113**. The support can include central bore **117**. In FIGS. 8G-H, fluted edges **110'** extend along sides **112'** to

US 10,314,742 B2

11

form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. **8E-H**, the support may contact the canal walls at at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. **8A-B** shows, some supports only have point contacts with the canal wall. For the supports shown in FIGS. **5B-C**, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. **6A-B** may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. **7D-E** that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. **8C-D**, in some variations, the support contacts the interior wall of the canal at at least two points; or at at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided FIGS. **9A-B**. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder **C** having length **L**, extending circumferentially from a first end **X₁** to a second end **X₂** of support **152**, and inside radius **R_i**. In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder **C** as described above. In other variations, the support contacts less than 10% of the surface area of **C**. In still other variations, the support contacts less than 30% of the surface area of **C**. For example, the support **152** shown in FIGS. **9A-B** contacts the canal wall **62** only at bead outer peripheral edges at **E₁-E₇**, along a distance of the bead width **B_{bp}**. There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmurial flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapeable metal having a sinusoidal or zig-zag configuration as shown FIGS. **8C-D**, a cross-sectional dimension **117** of the support can be decreased or increased by apply tension along dimension **119**. As illustrated in FIG. **10A**, a support **160** can extend essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately

12

half way around the circumference of the canal (not shown). As shown in FIG. **10B**, a support **162** can extend less than half way around the canal. As shown in FIG. **10C**, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. **11A**, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension **B_D**. Support **132** comprises a stiff arcuate element **135** with a radius of curvature **R_{supp}** smaller than the radius of curvature of Schlemm's canal **R_{SC}**. The smaller, fixed radius of curvature **R_{supp}** of arcuate member **135** urges canal **30** to open more than **B_D**. In other variations shown in FIGS. **11B** and **11D**, support **179** comprises an arcuate member **180** without beads having a radius of curvature **R_{supp}** that is less than the radius of curvature **R_{SC}** of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. **11C**, support **181** comprises an arcuate member **182** having a radius of curvature **R_{supp}** larger than that of Schlemm's canal **R_{SC}**. Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. **11C**, support **181** can include beads **184**. To urge open the canal, the radius of curvature **R_{supp}** of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal **R_{SC}**. For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member **R_{supp}** in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature **R_{supp}** of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at at least one point. Referring to FIG. **12A**, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. **12B** shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. **12C**, a front view of an arcuate support **210** is shown. FIG. **12D** shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. **12E**, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. **12F**. As illustrated in FIG. **12F**, bead **232** with fenestrations **234** occupies the majority of central core **67** of canal **30**. In other variations,

US 10,314,742 B2

13

the support occupies only a small portion of the central core of the canal. For example, in FIG. 12G, a front view of a support 240 having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. 12H.

A support can be made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacrylate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives, flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly(lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly(ethylene glycol) copolymer, a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer, a poly(lactic acid)/poly(ethylene glycol) copolymer, a poly(glycolic acid)/poly(ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone)/poly(ethylene glycol) copolymer, a poly(orthoester), a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a poly(anhydride), a poly(dioxanone), a poly(alkylene alkylate), a copolymer of polyethylene glycol and a polyorthoester, a biodegradable polyurethane, a poly(amino acid), a polyetherester, a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(e-caprolactone) dimethacrylate and n-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

14

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. 13, predetermined localized portions 120 of support 122 can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions 120 will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads 126 in support 120 are hollow, then after irradiation and ablation, features 120 will become fenestrations. The fenestrations can be created to make support 122 more porous in nature or to allow release of an active agent from within a support, e.g., from within beads 126. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source

US 10,314,742 B2

15

or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminescent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the support may be allowed to self-position in Schlemm's canal. In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

FIGS. 14A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. 14A, a support **200** can be introduced into the canal using syringe **202** and plunger **204**. Syringe **202** has distal end **206** that can be at

16

least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger **204**, thereby pushing support **200** into the canal. Referring to FIGS. 14B-C, distal end **208** of guide element **210** can be at least partially introduced into the canal. Guide element **210** can be a guide wire. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** comprises central bore **218** capable of accommodating guide element **210** such that support **212** can be threaded onto guide element **210** and slidably positioned along the guide element. Once distal end **209** of support **212** is threaded onto guide element **210**, support **212** can be pushed in a distal direction along guide element **210** to insert support **212** into the canal. In some variations, support **212** can remain threaded onto guide element **210**, and guide element **210** can remain in the canal. In other variations, support **212** can be slid off distal end **208** of guide element **210**, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. 14C-D, syringe **202** with plunger **204** can be used in combination with a guide element **210**. In this variation, distal end **208** of guide element **210** is inserted at least partially into Schlemm's canal. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** has central bore **218** capable of accommodating guide element **210**. Proximal end **211** of guide element **210** is inserted into bore **218**. Plunger **204** is depressed in a distal direction to push support **212** into the canal and slide support **212** along element **210**. Guide element **210** can remain in the canal or be removed following insertion of the support. Supports **200**, **212** must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

US 10,314,742 B2

17

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more mirrors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

18

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. 11A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

The invention claimed is:

1. A method for treating an eye condition, comprising: implanting a support within Schlemm's canal, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than the radius of curvature of Schlemm's canal such that at least a portion of the arcuate member extends out of Schlemm's canal.
2. The method of claim 1, wherein the support has at least one fenestration.
3. The method of claim 1, wherein the support has a length equal to about a quarter or less than a quarter of the circumference of Schlemm's canal.
4. The method of claim 1, wherein at least a portion of the support is made from a biocompatible polymer.
5. The method of claim 4, wherein the biocompatible polymer comprises a biodegradable polymer.
6. The method of claim 1, wherein at least a portion of the support is made from a shape memory material.
7. The method of claim 6, wherein the shape memory material comprises a shape memory alloy.
8. The method of claim 7, wherein the shape memory alloy comprises a nickel titanium alloy.
9. The method of claim 1, wherein at least a portion of the support is made from a biocompatible metal.
10. The method of claim 9, wherein the metal is titanium.
11. The method of claim 1, wherein at least a portion of the support is hollow.
12. The method of claim 1, wherein at least a portion of the support is porous.
13. The method of claim 1, wherein when the support is disposed within a cylindrical section of the lumen of

US 10,314,742 B2

19

20

Schlemm's canal having an internal wall surface area C, the support contacts less than 30% of C.

14. The method of claim **1**, wherein when the support is disposed within a cylindrical section of the lumen of Schlemm's canal having an internal wall surface area C, the support contacts less than 10% of C.

15. The method of claim **1**, wherein the support is flexible.

16. The method of claim **1**, wherein the support is rigid.

17. The method of claim **1**, wherein the support does not substantially interfere with longitudinal flow along Schlemm's canal.

18. The method of claim **1**, wherein the support does not substantially interfere with transmural flow into and out of Schlemm's canal.

19. The method of claim **1**, further comprising preloading the support into an introducer and delivering the support from the introducer into Schlemm's canal.

20. The method of claim **19**, wherein the support is delivered from the introducer using a pusher.

* * * * *

20

EXHIBIT E



US011389328B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.:** **US 11,389,328 B2**

(45) **Date of Patent:** ***Jul. 19, 2022**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

(58) **Field of Classification Search**

CPC A61F 9/00781; A61F 2210/0014; A61F 2250/0067

(71) Applicant: **Sight Sciences, Inc.**, Menlo Park, CA (US)

(Continued)

(56)

References Cited

U.S. PATENT DOCUMENTS

3,159,161 A 12/1964 Ness
4,068,664 A 1/1978 Sharp et al.

(Continued)

(73) Assignee: **SIGHT SCIENCES, INC.**, Menlo Park, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 656 days.

This patent is subject to a terminal disclaimer.

FOREIGN PATENT DOCUMENTS

CA 2778452 A1 4/2011
CN 1678407 A 10/2005

(Continued)

OTHER PUBLICATIONS

(21) Appl. No.: **16/413,466**

Final Office Action dated Jun. 9, 2020, for U.S. Appl. No. 15/854,126, filed Dec. 26, 2017, 9 pages.

(22) Filed: **May 15, 2019**

(Continued)

(65) **Prior Publication Data**

US 2020/0038243 A1 Feb. 6, 2020

Primary Examiner — Leslie R Deak

(74) *Attorney, Agent, or Firm* — Cooley LLP

(57)

ABSTRACT

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmurial fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmurial fluid flow across the canal.

Related U.S. Application Data

(60) Continuation of application No. 15/182,165, filed on Jun. 14, 2016, now Pat. No. 10,314,742, which is a (Continued)

(51) **Int. Cl.**

A61F 9/007 (2006.01)

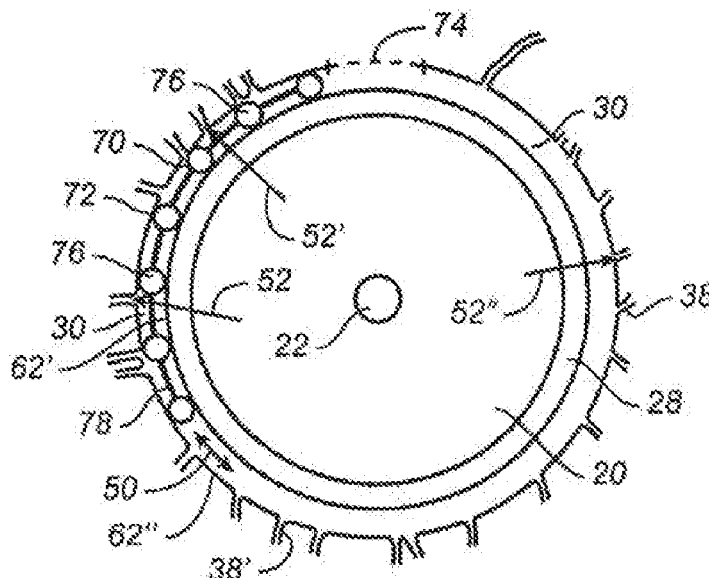
A61F 9/00 (2006.01)

(52) **U.S. Cl.**

CPC **A61F 9/00781** (2013.01); **A61F 9/0017** (2013.01); **A61F 2210/0004** (2013.01);

(Continued)

27 Claims, 16 Drawing Sheets



US 11,389,328 B2

Page 2

Related U.S. Application Data			7,909,789 B2 *	3/2011	Badawi A61F 9/0017 604/9
continuation of application No. 13/025,112, filed on			7,951,155 B2	5/2011	Smedley et al.
Feb. 10, 2011, now Pat. No. 9,370,443, which is a			7,967,772 B2	6/2011	McKenzie et al.
division of application No. 11/475,523, filed on Jun.			8,034,105 B2	10/2011	Stegmann et al.
26, 2006, now Pat. No. 7,909,789.			8,075,511 B2	12/2011	Tu et al.
(52)	U.S. Cl.	CPC A61F 2210/0014 (2013.01); A61F 2250/0067 (2013.01)	8,109,896 B2	2/2012	Nissan et al.
			8,123,729 B2	2/2012	Yamamoto et al.
			8,133,208 B2	3/2012	Hetherington
			8,137,307 B2	3/2012	Tennican et al.
			8,152,752 B2	4/2012	Lynch et al.
			8,172,899 B2	5/2012	Silvestrini et al.
			8,267,882 B2	9/2012	Euteneuer et al.
			8,273,050 B2	9/2012	Bergheim et al.
			8,282,592 B2	10/2012	Schieber et al.
			8,287,482 B2	10/2012	Badawi et al.
(58)	Field of Classification Search	USPC 604/8, 9, 264; 623/23.64, 23.7 See application file for complete search history.	8,333,742 B2	12/2012	Bergheim et al.
			8,337,509 B2	12/2012	Schieber et al.
			8,348,924 B2	1/2013	Christian et al.
			8,366,653 B2	2/2013	Shareef et al.
			8,372,026 B2	2/2013	Schieber et al.
			8,388,568 B2	3/2013	Lynch et al.
			8,403,920 B2	3/2013	Lind et al.
			8,414,518 B2	4/2013	Schieber et al.
			8,425,449 B2	4/2013	Wardle et al.
			8,425,450 B2	4/2013	Wilcox
(56)	References Cited	U.S. PATENT DOCUMENTS	8,439,972 B2	5/2013	Badawi et al.
			8,444,589 B2	5/2013	Silvestrini
			8,491,549 B2	7/2013	Conston et al.
			8,512,321 B2	8/2013	Baerveldt et al.
			8,512,404 B2	8/2013	Frion et al.
			8,529,622 B2	9/2013	Badawi et al.
			8,540,659 B2	9/2013	Berlin
			8,540,681 B2	9/2013	Hetherington
			8,545,431 B2	10/2013	Rickard
			8,568,391 B2	10/2013	Kearns et al.
			8,617,094 B2	12/2013	Smedley et al.
			8,657,776 B2	2/2014	Wardle et al.
			8,663,150 B2	3/2014	Wardle et al.
			8,715,266 B2	5/2014	Bos
			8,734,377 B2	5/2014	Schieber et al.
			8,747,299 B2	6/2014	Grieshaber
			8,771,217 B2	7/2014	Lynch et al.
			8,801,648 B2	8/2014	Bergheim et al.
			8,808,222 B2	8/2014	Schieber et al.
			8,827,990 B2	9/2014	Van Valen et al.
			8,852,137 B2	10/2014	Horvath et al.
			8,876,898 B2	11/2014	Badawi et al.
			8,888,734 B2	11/2014	Nissan et al.
			8,894,603 B2	11/2014	Badawi et al.
			8,926,546 B2	1/2015	Wilcox
			8,961,447 B2	2/2015	Schieber et al.
			9,039,650 B2	5/2015	Schieber et al.
			9,044,301 B1	6/2015	Pinchuk et al.
			9,050,169 B2	6/2015	Schieber et al.
			9,066,750 B2	6/2015	Wardle et al.
			9,066,783 B2	6/2015	Euteneuer et al.
			9,095,412 B2	8/2015	Badawi et al.
			9,107,729 B2	8/2015	Sorensen et al.
			9,125,723 B2	9/2015	Horvath et al.
			9,155,655 B2	10/2015	Schieber et al.
			9,192,516 B2	11/2015	Horvath et al.
			9,211,213 B2	12/2015	Wardle et al.
			9,216,109 B2	12/2015	Badawi et al.
			9,220,632 B2	12/2015	Smedley et al.
			9,226,850 B2	1/2016	Baerveldt et al.
			9,226,852 B2	1/2016	Schieber et al.
			9,301,875 B2	4/2016	Tu et al.
			9,326,891 B2	5/2016	Horvath et al.
			9,339,514 B2	5/2016	Bos et al.
			9,351,874 B2	5/2016	Schieber et al.
			9,358,155 B2	6/2016	Sorensen et al.
			9,358,156 B2	6/2016	Wardle et al.
			9,370,443 B2 *	6/2016	Badawi A61F 9/00781
			9,381,111 B2	7/2016	Hickingbotham et al.
			9,402,767 B2	8/2016	Schieber et al.
			9,486,361 B2 *	11/2016	Badawi A61F 9/0017
			9,492,319 B2	11/2016	Grieshaber et al.
			9,492,320 B2	11/2016	Lynch et al.

US 11,389,328 B2

Page 3

(56)

References Cited

U.S. PATENT DOCUMENTS

9,510,973 B2	12/2016	Wardle	2009/0132040 A1	5/2009	Frion et al.
9,855,167 B2	1/2018	Badawi et al.	2009/0227934 A1	9/2009	Euteneuer et al.
9,889,258 B2	2/2018	Bengtsson et al.	2009/0247955 A1	10/2009	Yamamoto et al.
9,895,258 B2	2/2018	Badawi et al.	2009/0287143 A1	11/2009	Line
10,179,066 B2	1/2019	Badawi et al.	2009/0287233 A1	11/2009	Huculak
10,299,958 B2	5/2019	Badawi et al.	2010/0019177 A1	1/2010	Luckevich
10,314,742 B2*	6/2019	Badawi A61F 9/0017	2010/0087774 A1	4/2010	Haffner et al.
10,398,597 B2	9/2019	Badawi et al.	2010/0121248 A1	5/2010	Yu et al.
10,406,030 B2	9/2019	Badawi et al.	2010/0173866 A1	7/2010	Hee et al.
10,857,027 B2	12/2020	Badawi et al.	2010/0179652 A1	7/2010	Yamamoto et al.
10,888,453 B2	1/2021	Badawi et al.	2010/0222802 A1	9/2010	Gillespie
11,090,188 B2	8/2021	Badawi et al.	2010/0241046 A1	9/2010	Pinchuk et al.
11,116,660 B2	9/2021	Badawi et al.	2010/0262174 A1	10/2010	Sretavan et al.
11,166,847 B2	11/2021	Badawi et al.	2011/0009874 A1	1/2011	Wardle et al.
2001/0014788 A1	8/2001	Morris	2011/0009958 A1	1/2011	Wardle et al.
2002/0013546 A1	1/2002	Grieshaber et al.	2011/0098809 A1	4/2011	Wardle et al.
2002/0013572 A1	1/2002	Berlin	2011/0224597 A1	9/2011	Stegmann et al.
2002/0055753 A1	5/2002	Silvestrini	2011/0238009 A1	9/2011	Meron et al.
2002/0072673 A1	6/2002	Yamamoto et al.	2011/0238075 A1	9/2011	Clauson et al.
2002/0133168 A1	9/2002	Smedley et al.	2011/0306915 A1	12/2011	De Juan, Jr. et al.
2002/0143284 A1	10/2002	Tu et al.	2012/0010702 A1	1/2012	Stegmann et al.
2003/0060447 A1	3/2003	Karakelle et al.	2012/0123315 A1	5/2012	Horvath et al.
2003/0060873 A1	3/2003	Gertner et al.	2012/0123434 A1	5/2012	Grabner et al.
2003/0120200 A1	6/2003	Bergheim et al.	2012/0136306 A1	5/2012	Bartha
2003/0181848 A1	9/2003	Bergheim et al.	2012/0165720 A1	6/2012	Horvath et al.
2003/0229303 A1	12/2003	Haffner et al.	2012/0191064 A1	7/2012	Conston et al.
2003/0236483 A1	12/2003	Ren	2012/0197175 A1	8/2012	Horvath et al.
2003/0236484 A1	12/2003	Lynch et al.	2012/0203160 A1	8/2012	Kahook et al.
2004/0044310 A1	3/2004	Suzuki	2012/0220917 A1	8/2012	Silvestrini et al.
2004/0193095 A1	9/2004	Shadduck	2012/0310072 A1	12/2012	Grieshaber
2004/0193262 A1	9/2004	Shadduck	2012/0310137 A1	12/2012	Silvestrini
2004/0210181 A1	10/2004	Vass et al.	2012/0325704 A1	12/2012	Kerns et al.
2004/0254519 A1	12/2004	Tu et al.	2013/0041346 A1	2/2013	Alon
2004/0254520 A1	12/2004	Porteous et al.	2013/0158462 A1	6/2013	Wardle et al.
2004/0254521 A1	12/2004	Simon	2013/0245600 A1	9/2013	Yamamoto et al.
2004/0260228 A1	12/2004	Lynch et al.	2013/0274655 A1	10/2013	Jennings et al.
2005/0055082 A1	3/2005	Ben Muvhar et al.	2014/0066833 A1	3/2014	Yaron et al.
2005/0101967 A1	5/2005	Weber et al.	2014/0081194 A1	3/2014	Burns et al.
2005/0171507 A1	8/2005	Christian	2014/0121584 A1	5/2014	Wardle et al.
2005/0192527 A1	9/2005	Gharib et al.	2014/0128847 A1	5/2014	Lopez
2005/0209549 A1	9/2005	Bergheim et al.	2014/0135916 A1	5/2014	Clauson et al.
2005/0250788 A1	11/2005	Tu et al.	2014/0163448 A1	6/2014	Lind et al.
2005/0266047 A1	12/2005	Tu et al.	2014/0171852 A1	6/2014	Khor
2005/0267555 A1	12/2005	Marnfeldt et al.	2014/0194916 A1	7/2014	Ichikawa
2005/0277864 A1	12/2005	Haffner et al.	2014/0213958 A1	7/2014	Clauson et al.
2005/0288619 A1	12/2005	Gharib et al.	2014/0236066 A1	8/2014	Horvath et al.
2006/0032507 A1	2/2006	Tu	2014/0276332 A1	9/2014	Crimaldi et al.
2006/0036207 A1	2/2006	Koonmen et al.	2014/0288485 A1	9/2014	Berlin
2006/0069340 A1	3/2006	Simon	2014/0309599 A1	10/2014	Schaller
2006/0074375 A1	4/2006	Bergheim et al.	2014/0364791 A1	12/2014	Stegmann et al.
2006/0084907 A1	4/2006	Bergheim et al.	2015/0005623 A1	1/2015	Grover et al.
2006/0149194 A1	7/2006	Conston	2015/0011926 A1	1/2015	Reitsamer et al.
2006/0155300 A1	7/2006	Stamper et al.	2015/0051699 A1	2/2015	Badawi et al.
2006/0173077 A1	8/2006	Cagle	2015/0065940 A1	3/2015	Rangel-Friedman et al.
2006/0173397 A1	8/2006	Tu et al.	2015/0080783 A1	3/2015	Berlin
2006/0173446 A1	8/2006	Dacquay et al.	2015/0112372 A1	4/2015	Perez Grossmann
2006/0195055 A1	8/2006	Bergheim et al.	2015/0119787 A1	4/2015	Wardle et al.
2006/0195056 A1	8/2006	Bergheim et al.	2015/0125328 A1	5/2015	Bourne et al.
2006/0195187 A1	8/2006	Stegmann et al.	2015/0133946 A1	5/2015	Horvath et al.
2006/0200113 A1	9/2006	Haffner et al.	2015/0148615 A1	5/2015	Brennan et al.
2006/0217741 A1	9/2006	Ghannoum	2015/0216729 A1	8/2015	Doci
2006/0241580 A1	10/2006	Mittelstein et al.	2015/0223981 A1	8/2015	Smedley et al.
2007/0073275 A1	3/2007	Conston et al.	2015/0223983 A1	8/2015	Schieber et al.
2007/0106236 A1	5/2007	Coroneo	2015/0250649 A1	9/2015	Euteneuer et al.
2007/0191863 A1	8/2007	De Juan, Jr. et al.	2015/0257932 A1	9/2015	Pinchuk et al.
2007/0260173 A1	11/2007	Boukhny et al.	2015/0282982 A1	10/2015	Schieber et al.
2007/0276420 A1	11/2007	Sorensen et al.	2015/0313758 A1	11/2015	Wilcox
2008/0004596 A1	1/2008	Yun et al.	2015/0320596 A1	11/2015	Gifford, III et al.
2008/0058704 A1	3/2008	Hee et al.	2015/0374545 A1	12/2015	Horvath et al.
2008/0058760 A1	3/2008	Agerup	2016/0022486 A1	1/2016	Clauson et al.
2008/0082078 A1	4/2008	Berlin	2016/0051408 A1	2/2016	Baerveldt et al.
2008/0300574 A1	12/2008	Belson et al.	2016/0095985 A1	4/2016	Novak
2009/0036819 A1	2/2009	Tu et al.	2016/0100980 A1	4/2016	Badawi et al.
2009/0043321 A1	2/2009	Conston et al.	2016/0106589 A1	4/2016	Mittelstein et al.
2009/0082862 A1	3/2009	Schieber et al.	2016/0135994 A1	5/2016	Romoda et al.
			2016/0143778 A1	5/2016	Aljuri et al.
			2016/0151204 A1	6/2016	Haffner et al.
			2016/0220417 A1	8/2016	Schieber et al.
			2016/0220418 A1	8/2016	Sorensen et al.

US 11,389,328 B2

Page 4

(56)

References Cited

U.S. PATENT DOCUMENTS

2016/0256317	A1	9/2016	Horvath et al.
2016/0256323	A1	9/2016	Horvath et al.
2016/0287438	A1	10/2016	Badawi et al.
2016/0302965	A1	10/2016	Erickson et al.
2016/0331588	A1	11/2016	Ambati et al.
2016/0346006	A1	12/2016	Hickengbotham et al.
2016/0354248	A1	12/2016	Kahook
2017/0202707	A1	7/2017	Badawi et al.
2017/0258507	A1	9/2017	Hetherington
2018/0271699	A1	9/2018	Badawi et al.
2019/0142632	A1	5/2019	Badawi et al.
2019/0314200	A1	10/2019	Badawi et al.
2020/0121503	A1	4/2020	Badawi et al.
2020/0129333	A1	4/2020	Badawi et al.
2021/0236333	A1	8/2021	Badawi et al.
2022/0104967	A1	4/2022	Badawi et al.
2022/0104968	A1	4/2022	Badawi et al.

FOREIGN PATENT DOCUMENTS

CN	101505830	A	8/2009
CN	102202706	A	9/2011
EP	2 830 553	B1	12/2017
JP	03-168154	A	7/1991
JP	2002-541976	A	12/2002
JP	2003-180730	A	7/2003
JP	2005-510317	A	4/2005
JP	2005-538809	A	12/2005
JP	2007-527251	A	9/2007
JP	2012-527318	A	11/2012
JP	2013-512707	A	4/2013
JP	2014-036867	A	2/2014
JP	2014-533600	A	12/2014
WO	WO-00/64393	A1	11/2000
WO	WO-03/045582	A1	6/2003
WO	WO-2004/026361	A1	4/2004
WO	WO-2004/069664	A2	8/2004
WO	WO-2004/069664	A3	8/2004
WO	WO-2005/105197	A2	11/2005
WO	WO-2005/105197	A3	11/2005
WO	WO-2005/107664	A2	11/2005
WO	WO-2005/107664	A3	11/2005
WO	WO-2005/117752	A1	12/2005
WO	WO-2006/066103	A2	6/2006
WO	WO-2006/066103	A3	6/2006
WO	WO-2008/002377	A1	1/2008
WO	WO-2009/042596	A2	4/2009
WO	WO-2009/042596	A3	4/2009
WO	WO-2011/097408	A1	8/2011
WO	WO-2011/106781	A1	9/2011
WO	WO-2013/141898	A1	9/2013
WO	WO-2016/042162	A1	3/2016
WO	WO-2016/159999	A1	10/2016

OTHER PUBLICATIONS

Final Office Action dated Jun. 9, 2020, for U.S. Appl. No. 16/189,882, filed Nov. 13, 2018, 12 pages.

Non-Final Office Action dated Nov. 25, 2019, for U.S. Appl. No. 16/189,882, filed Nov. 13, 2018, 12 pages.

Boyle, E.L. (Feb. 1, 2006). "New Glaucoma Devices Take Different Approaches to IOP Lowering," *Ocular Surgery News U.S. Edition*, located at <<http://www.osnsupersite.com/view.aspx?rid=12436>>, last visited on Apr. 23, 2012, 4 pages, revisited on Apr. 19, 2016, 5 pages.

Corrected Notice of Allowability dated Nov. 23, 2018, for U.S. Appl. No. 14/816,822, filed Aug. 3, 2015, 2 pages.

Corrected Notice of Allowability dated Dec. 12, 2018, for U.S. Appl. No. 14/816,822, filed Aug. 3, 2015, 2 pages.

Corrected Notice of Allowability dated Feb. 21, 2019, for U.S. Appl. No. 14/675,580, filed Mar. 31, 2015, 6 pages.

Corrected Notice of Allowability dated Apr. 3, 2019, for U.S. Appl. No. 14/675,580, filed Mar. 31, 2015, 3 pages.

Extended European Search Report dated Apr. 22, 2015, for EP Patent Application No. 11 740 372.5, filed Feb. 3, 2011, six pages.

Extended European Search Report dated Jun. 9, 2016, for European Patent Application No. 16 155 079.3, filed on May 31, 2007, 7 pages.

Extended European Search Report dated May 17, 2011, for European Patent Application No. 11 162 487.0, filed on May 31, 2007, 6 pages.

Extended European Search Report dated Mar. 24, 2016, for European Patent Application No. 12 871 982.0, filed on Oct. 4, 2012, 7 pages.

Extended European Search Report dated Nov. 20, 2018, for European Patent Application No. 15 888 007.0, filed on Mar. 31, 2015, 9 pages.

Final Office Action dated Nov. 1, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 12 pages.

Final Office Action dated Jul. 19, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 6 pages.

Final Office Action dated Feb. 1, 2013, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 6 pages.

Final Office Action dated Sep. 15, 2014, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 13 pages.

Final Office Action dated Sep. 20, 2013, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 16 pages.

Final Office Action dated Nov. 12, 2013, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 8 pages.

Final Office Action dated Jan. 8, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 8 pages.

Final Office Action dated Sep. 3, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 8 pages.

Final Office Action dated Apr. 23, 2015, for U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 8 pages.

Final Office Action dated Aug. 19, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 6 pages.

Final Office Action dated Mar. 9, 2016, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 11 pages.

Final Office Action dated Oct. 3, 2016, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 27 pages.

Final Office Action dated May 18, 2017, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 14 pages.

Final Office Action dated Jan. 29, 2018, for U.S. Appl. No. 14/973,620, filed Dec. 17, 2015, 19 pages.

Final Office Action dated Apr. 6, 2018, for U.S. Appl. No. 15/683,652, filed Aug. 22, 2017, 11 pages.

Final Office Action dated Jun. 1, 2018, for U.S. Appl. No. 14/816,822, filed Aug. 3, 2015, 6 pages.

Final Office Action dated Oct. 19, 2018, for U.S. Appl. No. 15/683,652, filed Aug. 22, 2017, 8 pages.

Final Office Action dated Apr. 19, 2019, for U.S. Appl. No. 14/973,620, filed Dec. 17, 2015, 12 pages.

International Search Report dated Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, 4 pages.

International Search Report dated Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 2 pages.

International Search Report dated Feb. 1, 2013 for PCT Application No. PCT/US2012/058751, filed on Oct. 4, 2012, 4 pages.

International Search Report dated Sep. 14, 2015, for PCT Application No. PCT/US2015/023720, filed on Mar. 31, 2015, 5 pages.

Non-Final Office Action dated May 17, 2010, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 10 pages.

Non-Final Office Action dated Jan. 26, 2012, for U.S. Appl. No. 12/695,053, filed Jan. 27, 2010, 10 pages.

Non-Final Office Action dated Mar. 15, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 4 pages.

Non-Final Office Action dated May 11, 2012, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 5 pages.

Non-Final Office Action dated Nov. 9, 2012, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 5 pages.

Non-Final Office Action dated Apr. 24, 2013, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 13 pages.

Non-Final Office Action dated Jun. 12, 2013, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 8 pages.

US 11,389,328 B2

Page 5

(56)

References Cited

OTHER PUBLICATIONS

Non-Final Office Action dated Sep. 9, 2013, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.
Non-Final Office Action dated Feb. 7, 2014, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 12 pages.
Non-Final Office Action dated Feb. 24, 2014, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 12 pages.
Non-Final Office Action dated May 15, 2014, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.
Non-Final Office Action dated Nov. 28, 2014, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 7 pages.
Non-Final Office Action dated Jan. 14, 2015, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 10 pages.
Non-Final Office Action dated Feb. 4, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 6 pages.
Non-Final Office Action dated Feb. 23, 2015, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 17 pages.
Non-Final Office Action dated Jul. 10, 2015, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 16 pages.
Non-Final Office Action dated Oct. 7, 2015, U.S. for U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 5 pages.
Non-Final Office Action dated Nov. 3, 2015, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 7 pages.
Non-Final Office Action dated Dec. 14, 2015, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 7 pages.
Non-Final Office Action dated Jun. 7, 2016, for U.S. Appl. No. 14/527,292, filed Oct. 29, 2014, 5 pages.
Non-Final Office Action dated Feb. 25, 2016, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 19 pages.
Non-Final Office Action dated Jan. 18, 2017, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 13 pages.
Non-Final Office Action dated Mar. 22, 2017, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 31 pages.
Non-Final Office Action dated Aug. 28, 2017, for U.S. Appl. No. 14/973,620, filed Dec. 17, 2015, 6 pages.
Non-Final Office Action dated Nov. 7, 2017, for U.S. Appl. No. 14/816,822, filed Aug. 3, 2015, 14 pages.
Non-Final Office Action dated Dec. 15, 2017, for U.S. Appl. No. 15/343,147, filed on Nov. 3, 2016, 12 pages.
Non-Final Office Action dated Apr. 4, 2018, for U.S. Appl. No. 14/675,580, filed Mar. 31, 2015, 10 pages.
Non-Final Office Action dated Aug. 9, 2018, for U.S. Appl. No. 15/182,165, filed Jun. 14, 2016, 9 pages.
Non-Final Office Action dated Aug. 29, 2018, for U.S. Appl. No. 14/973,620, filed Dec. 17, 2015, 11 pages.
Non-Final Office Action dated Sep. 20, 2018, for U.S. Appl. No. 15/340,911, filed Nov. 1, 2016, 7 pages.
Non-Final Office Action dated Oct. 7, 2019, for U.S. Appl. No. 15/854,126, filed Dec. 26, 2017, 13 pages.
Notice of Allowance dated Feb. 2, 2011, for U.S. Appl. No. 11/475,523, filed Jun. 26, 2006, 6 pages.
Notice of Allowance dated Jun. 11, 2012, for U.S. Appl. No. 12/695,053, filed Jan. 27, 2010, 7 pages.
Notice of Allowance dated Apr. 2, 2013, for U.S. Appl. No. 13/245,811, filed Sep. 26, 2011, 6 pages.
Notice of Allowance dated May 10, 2013, for U.S. Appl. No. 13/020,706, filed Feb. 3, 2011, 8 pages.
Notice of Allowance dated Jul. 7, 2014, for U.S. Appl. No. 14/012,963, filed Aug. 28, 2013, 6 pages.
Notice of Allowance dated Jul. 23, 2014, for U.S. Appl. No. 13/644,780, filed Oct. 4, 2012, 8 pages.
Notice of Allowance dated Mar. 30, 2015, for U.S. Appl. No. 13/644,748, filed Oct. 4, 2012, 5 pages.

Notice of Allowance dated Aug. 10, 2015, for U.S. Appl. No. 13/644,758, filed Oct. 4, 2012, 7 pages.
Notice of Allowance dated Mar. 1, 2016, for U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 7 pages.
Corrected Notice of Allowability dated Apr. 25, 2016, U.S. Appl. No. 13/025,112, filed Feb. 10, 2011, 2 pages.
Notice of Allowance dated Jul. 13, 2016, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 7 pages.
Corrected Notice of Allowability dated Sep. 1, 2016, for U.S. Appl. No. 13/445,816, filed Apr. 12, 2012, 2 pages.
Notice of Allowance dated Oct. 25, 2017, for U.S. Appl. No. 13/644,769, filed Oct. 4, 2012, 8 pages.
Notice of Allowance dated Nov. 21, 2017, for U.S. Appl. No. 14/539,648, filed Nov. 12, 2014, 10 pages.
Notice of Allowance dated Aug. 31, 2018, for U.S. Appl. No. 14/816,822, filed Aug. 3, 2015, 7 pages.
Notice of Allowance dated Jan. 9, 2019, for U.S. Appl. No. 14/675,580, filed Mar. 31, 2015, 9 pages.
Notice of Allowance dated Feb. 6, 2019, for U.S. Appl. No. 15/182,165, filed Jun. 14, 2016, 8 pages.
Notice of Allowance dated Apr. 15, 2019, for U.S. Appl. No. 15/683,652, filed Aug. 22, 2017, 5 pages.
Notice of Allowance dated Apr. 23, 2019, for U.S. Appl. No. 15/340,911, filed Nov. 1, 2016, 5 pages.
Written Opinion dated Nov. 30, 2007, for PCT Application No. PCT/US2007/013038, filed on May 31, 2007, 6 pages.
Written Opinion dated Apr. 5, 2011, for PCT Application No. PCT/US2011/023643, filed on Feb. 3, 2011, 5 pages.
Written Opinion dated Feb. 1, 2013 for PCT Application No. PCT/US2012/058751, filed on Oct. 4, 2012, 6 pages.
Written Opinion dated Sep. 14, 2015 for PCT Application No. PCT/US15/23720, filed on Mar. 31, 2015, 8 pages.
Corrected Notice of Allowability dated Oct. 12, 2021, for U.S. Appl. No. 16/532,260, filed Aug. 5, 2019, 2 pages.
Corrected Notice of Allowability dated Apr. 15, 2022, for U.S. Appl. No. 17/239,270, filed Apr. 23, 2021, 2 pages.
Final Office Action dated Apr. 1, 2021, for U.S. Appl. No. 16/532,260, filed Aug. 5, 2019, 8 pages.
Final Office Action dated Dec. 21, 2021, for U.S. Appl. No. 17/239,270, filed Apr. 23, 2021, 14 pages.
Non-Final Office Action dated Aug. 10, 2020, for U.S. Appl. No. 14/973,620, filed Dec. 17, 2015, 8 pages.
Non-Final Office Action dated Oct. 1, 2020, for U.S. Appl. No. 16/397,733, filed Apr. 29, 2019, 7 pages.
Non-Final Office Action dated Jul. 15, 2021, for U.S. Appl. No. 17/239,263, filed Apr. 23, 2021, 9 pages.
Non-Final Office Action dated Aug. 26, 2021, for U.S. Appl. No. 17/239,270, filed Apr. 23, 2021, 21 pages.
Non-Final Office Action dated Mar. 4, 2022, for U.S. Appl. No. 17/553,671, filed Dec. 16, 2021, 9 pages.
Non-Final Office Action dated Mar. 10, 2022, for U.S. Appl. No. 17/553,408, filed Dec. 16, 2021, 18 pages.
Notice of Allowance dated Aug. 20, 2020, for U.S. Appl. No. 16/189,882, filed Nov. 13, 2018, 8 pages.
Notice of Allowance dated Sep. 16, 2020, for U.S. Appl. No. 15/854,126, filed Dec. 26, 2017, 9 pages.
Notice of Allowance dated Aug. 2, 2021, for U.S. Appl. No. 17/239,263, filed Apr. 23, 2021, 5 pages.
Notice of Allowance dated Sep. 17, 2021, for U.S. Appl. No. 16/532,260, filed Aug. 5, 2019, 9 pages.
Notice of Allowance dated Mar. 15, 2022, for U.S. Appl. No. 17/239,270, filed Apr. 23, 2021, 8 pages.

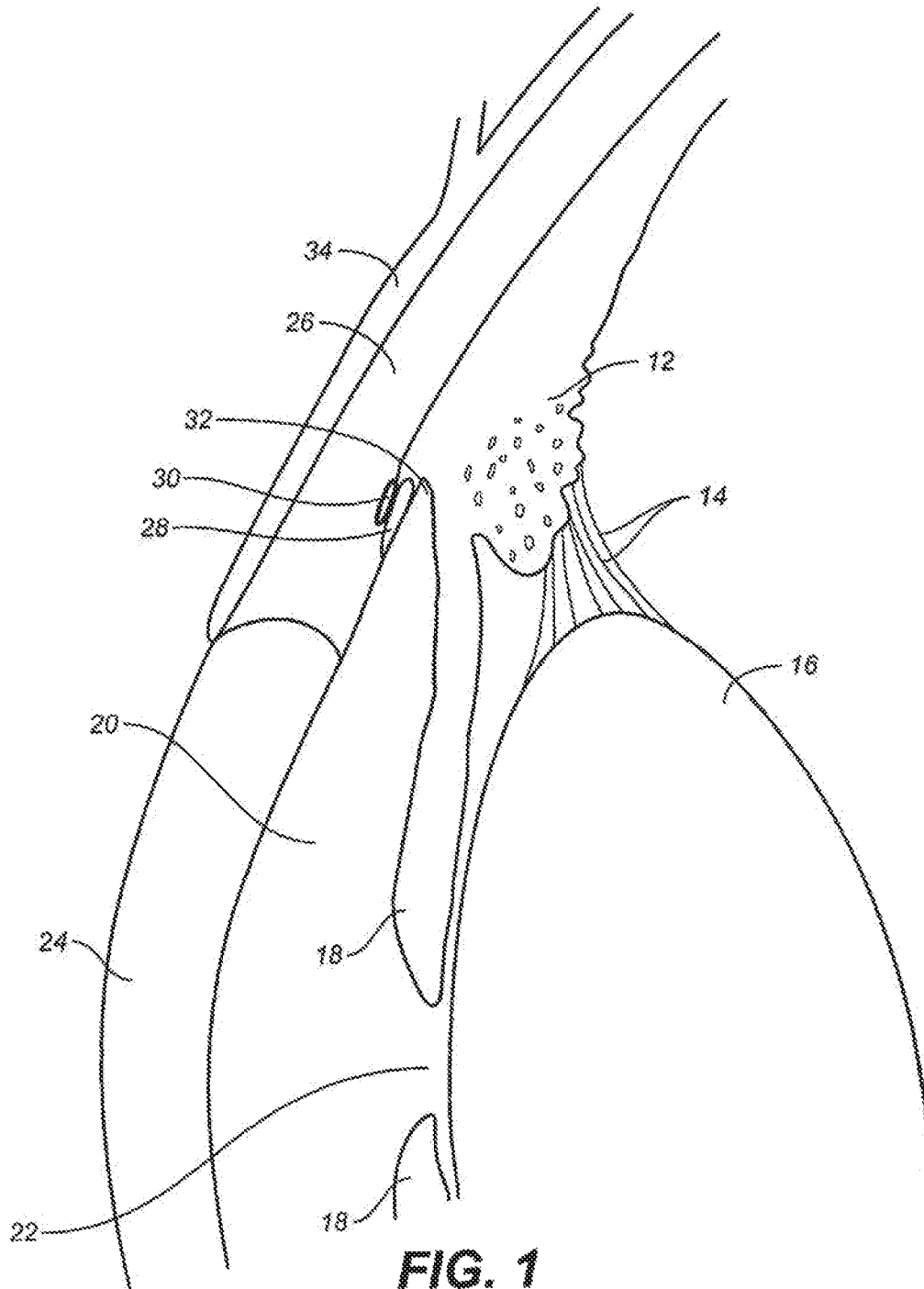
* cited by examiner

U.S. Patent

Jul. 19, 2022

Sheet 1 of 16

US 11,389,328 B2

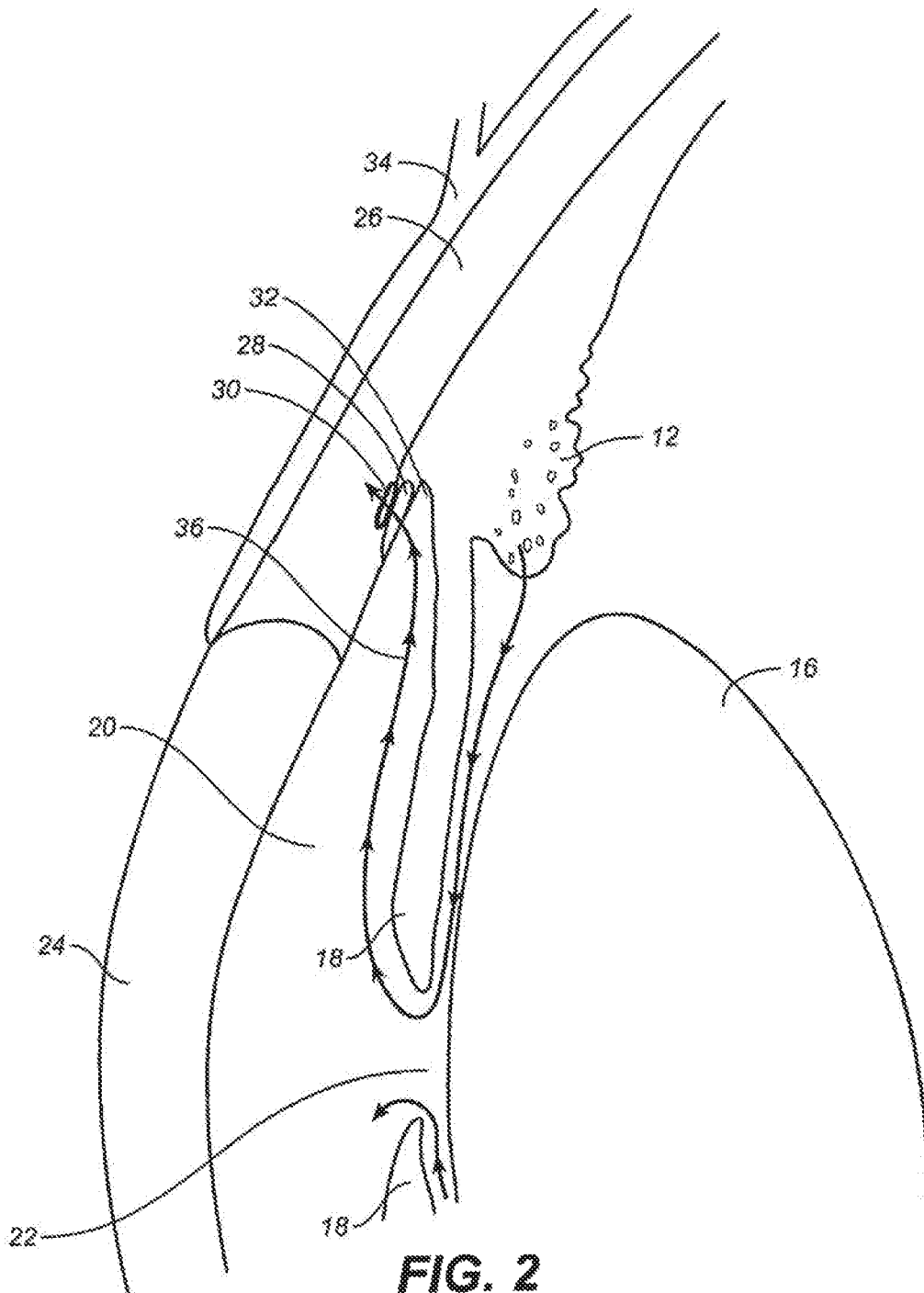


U.S. Patent

Jul. 19, 2022

Sheet 2 of 16

US 11,389,328 B2



U.S. Patent

Jul. 19, 2022

Sheet 3 of 16

US 11,389,328 B2

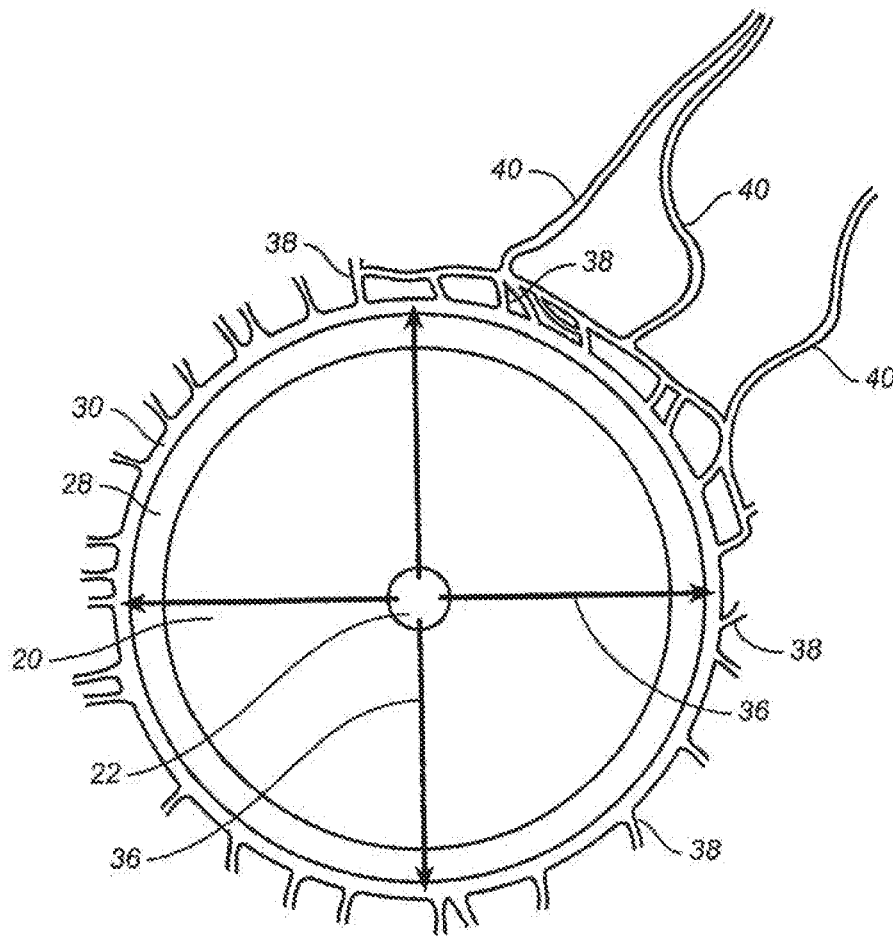


FIG. 3

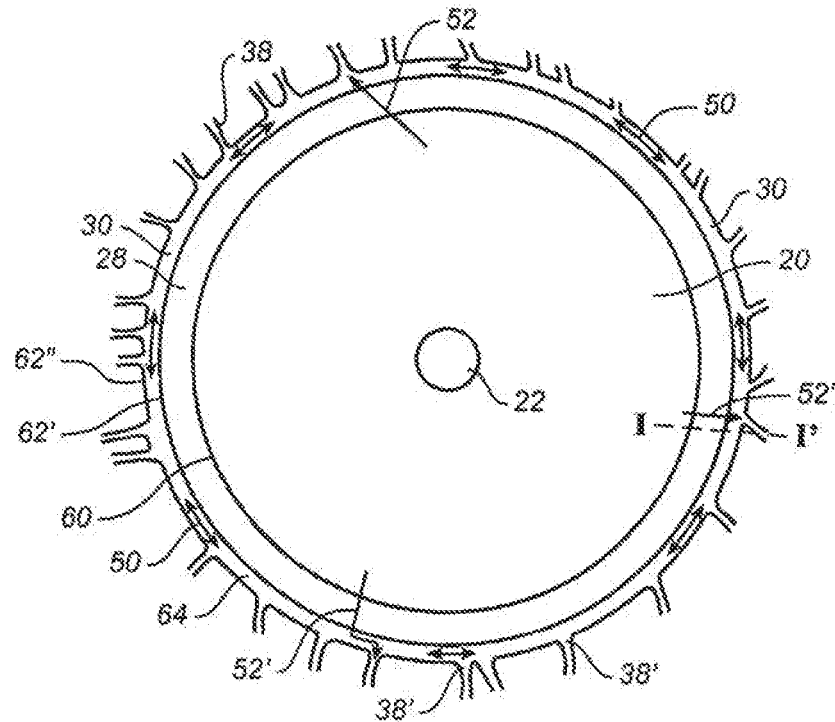


FIG. 4A

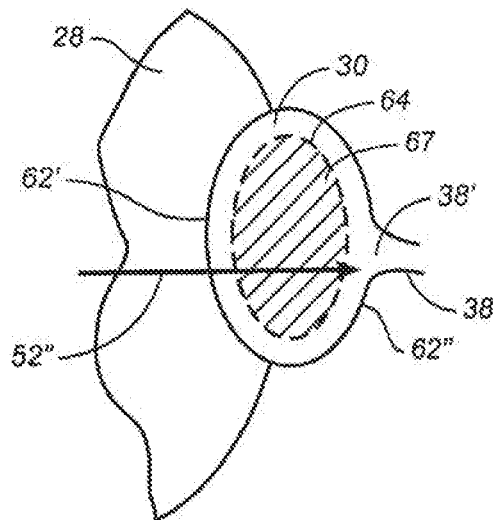


FIG. 4B

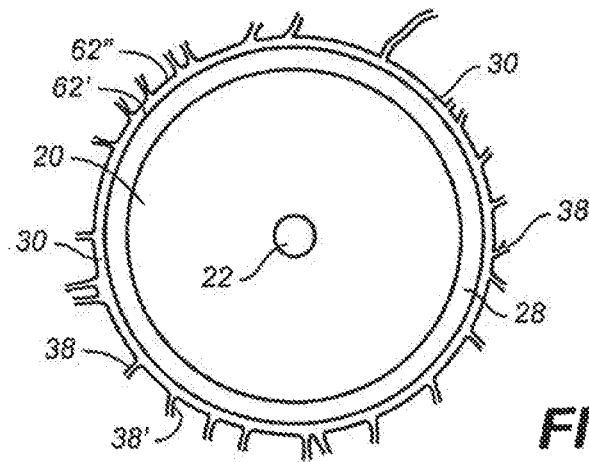


FIG. 5A

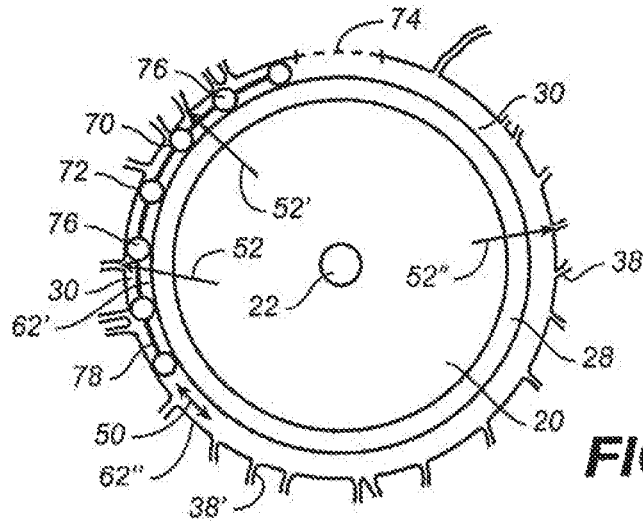


FIG. 5B

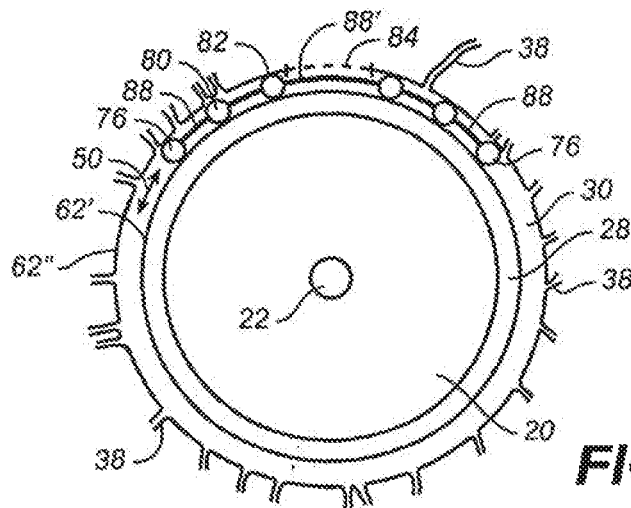


FIG. 5C

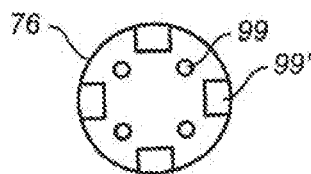
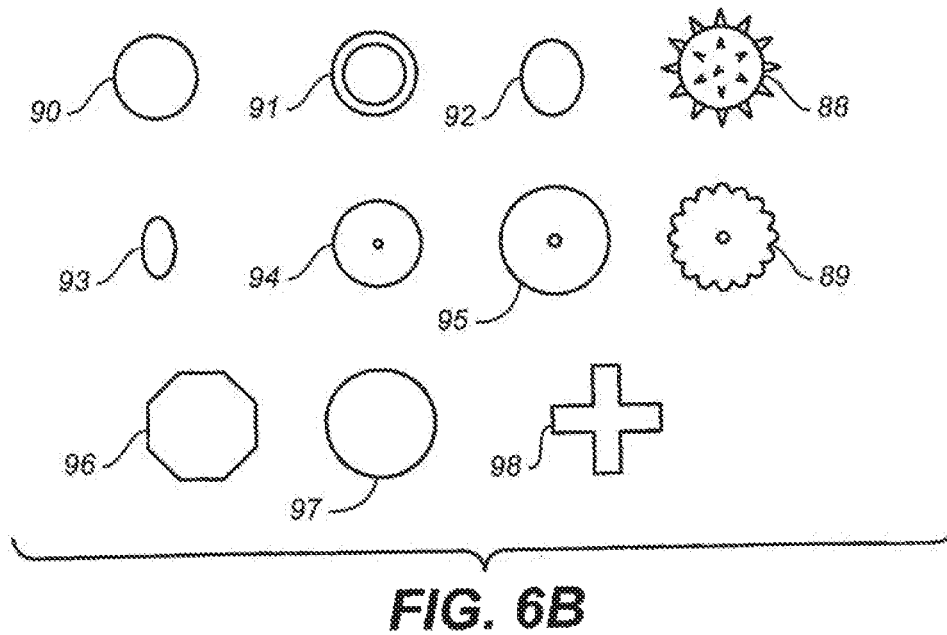
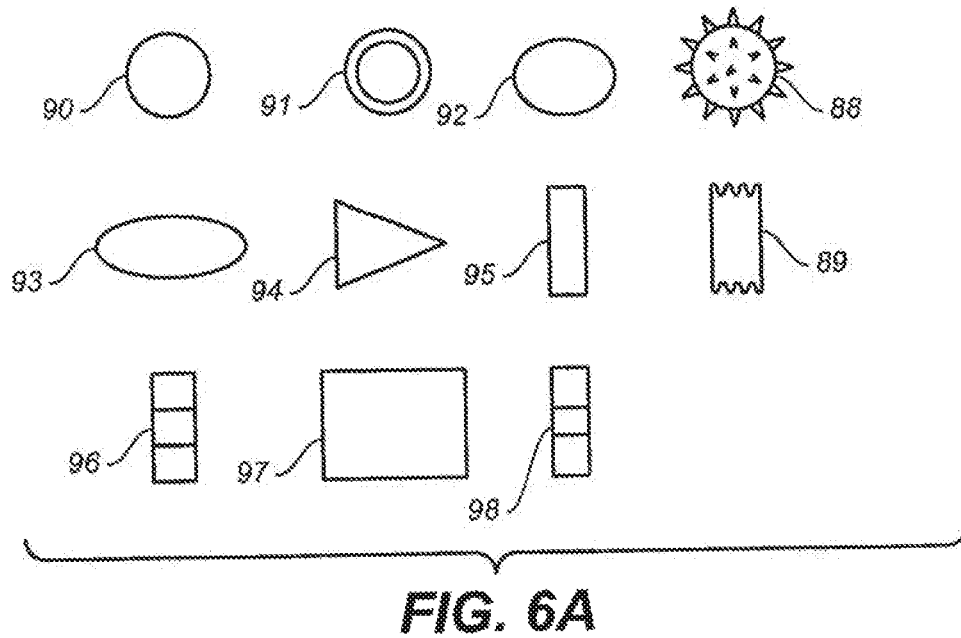


FIG. 6C



FIG. 7A



FIG. 7B

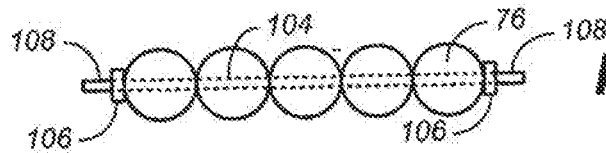


FIG. 7C

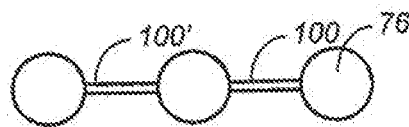


FIG. 7D

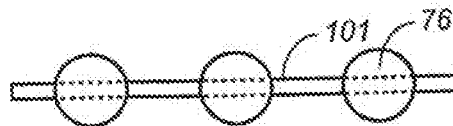


FIG. 7E

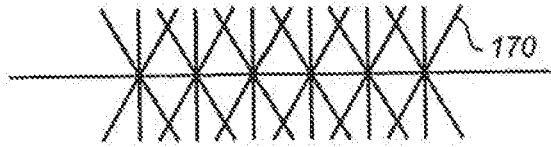


FIG. 8A

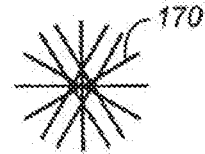


FIG. 8B

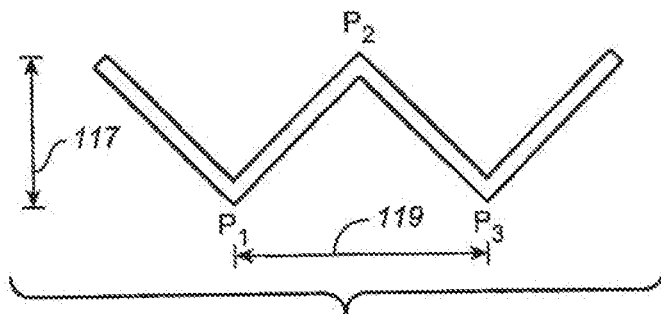


FIG. 8C

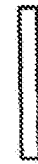


FIG. 8D

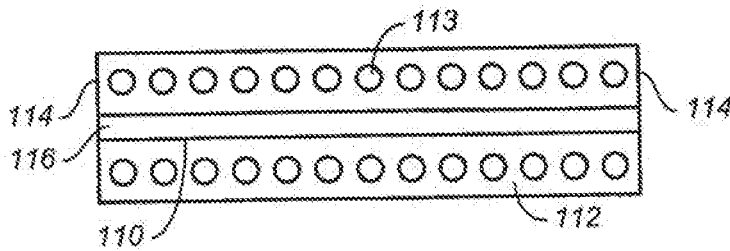


FIG. 8E

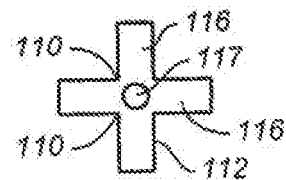


FIG. 8F

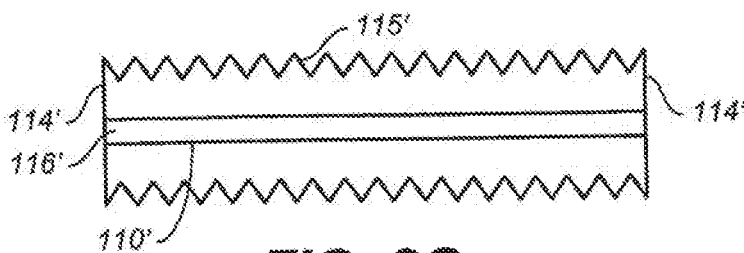


FIG. 8G

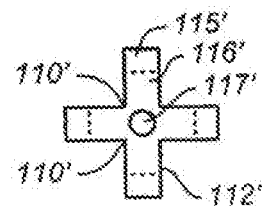


FIG. 8H

U.S. Patent

Jul. 19, 2022

Sheet 9 of 16

US 11,389,328 B2

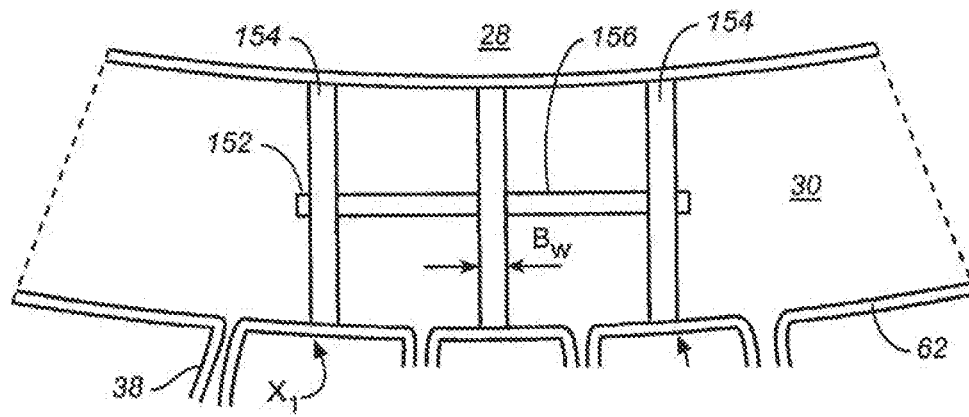


FIG. 9A

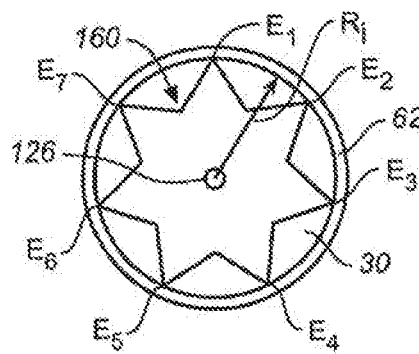


FIG. 9B

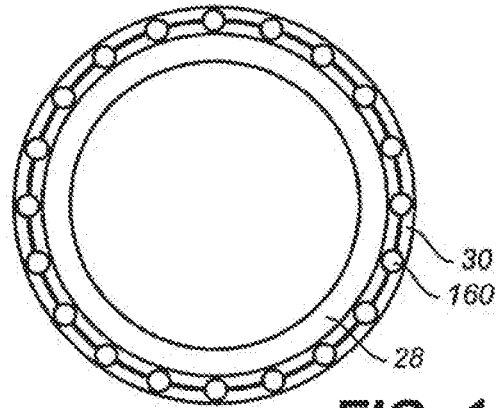


FIG. 10A

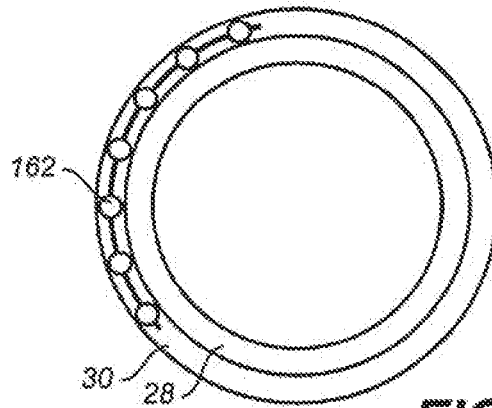


FIG. 10B

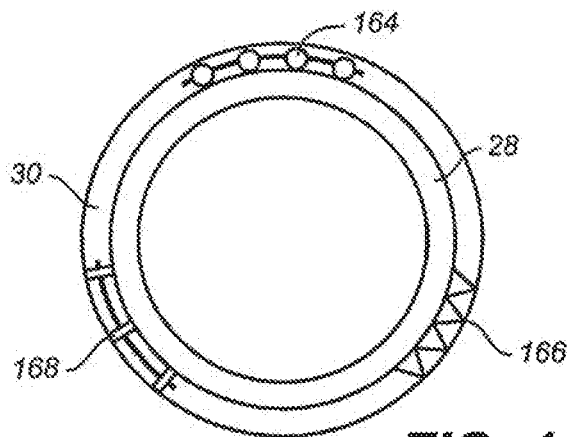


FIG. 10C

U.S. Patent

Jul. 19, 2022

Sheet 11 of 16

US 11,389,328 B2

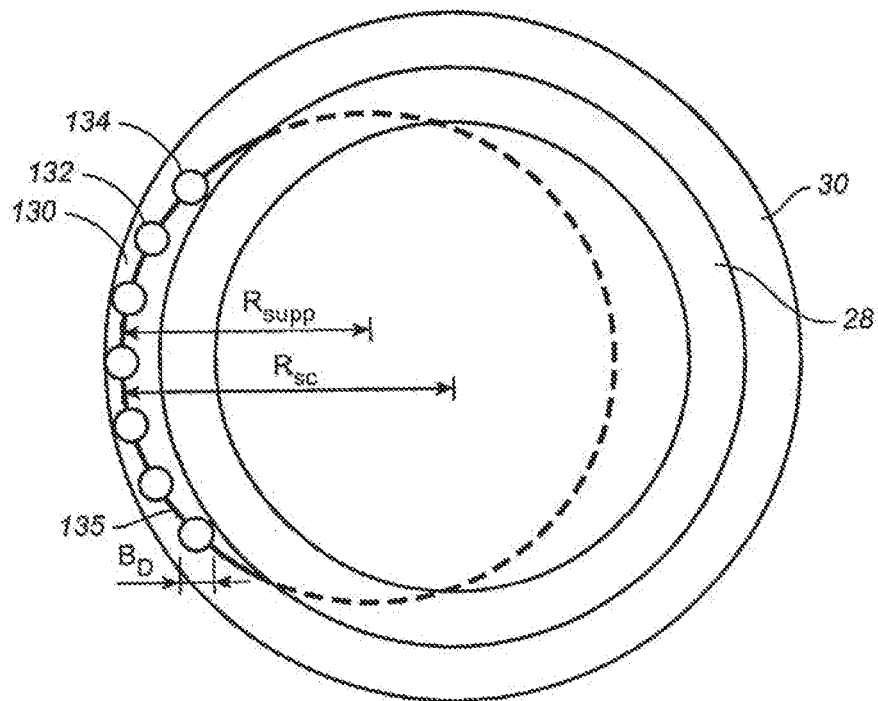


FIG. 11A

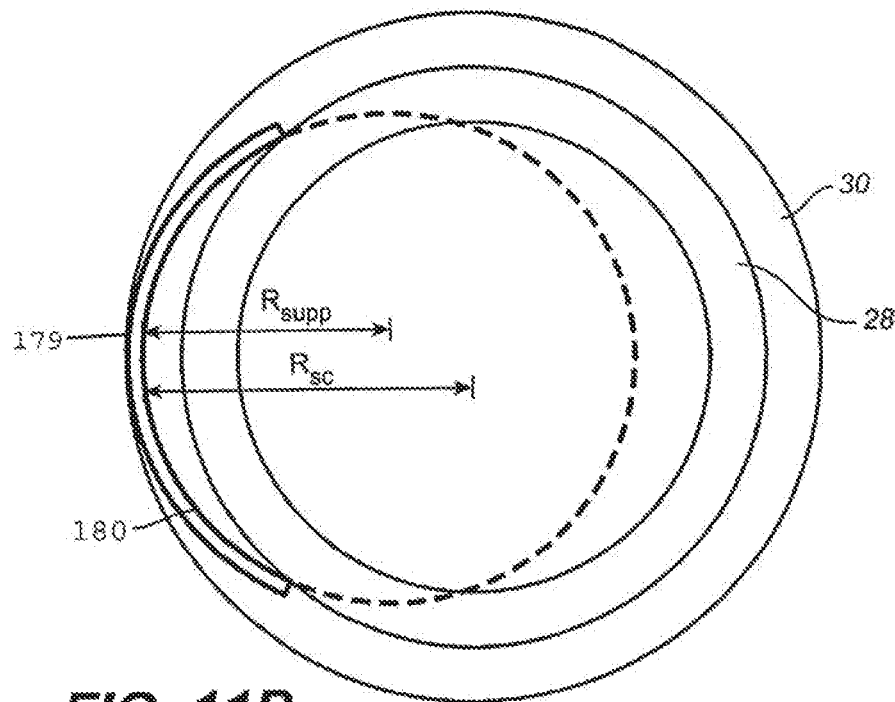


FIG. 11B

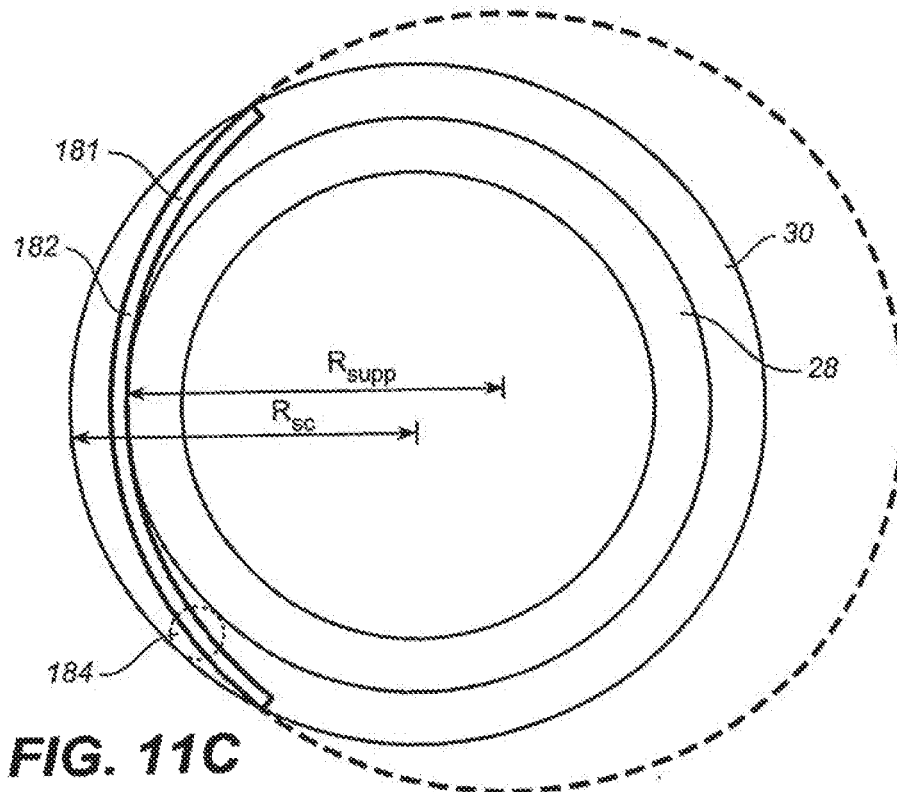


FIG. 11C

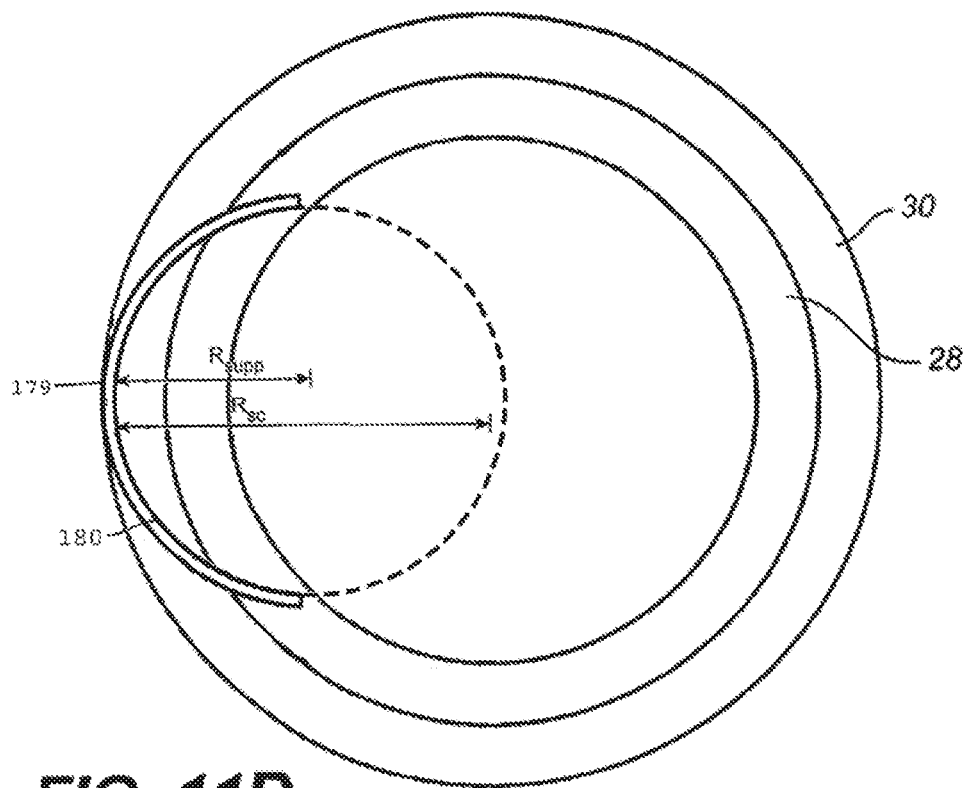


FIG. 11D

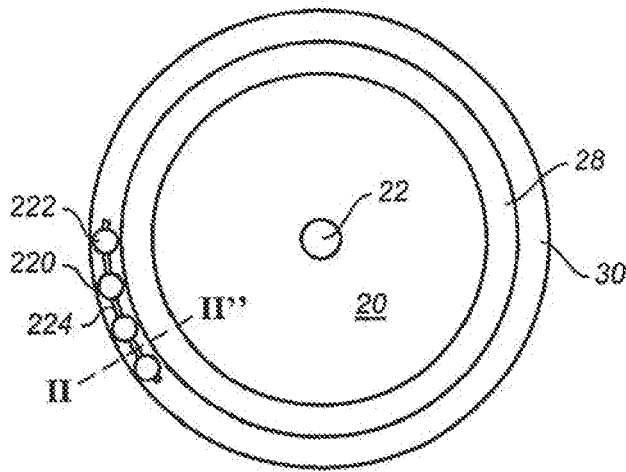


FIG. 12A

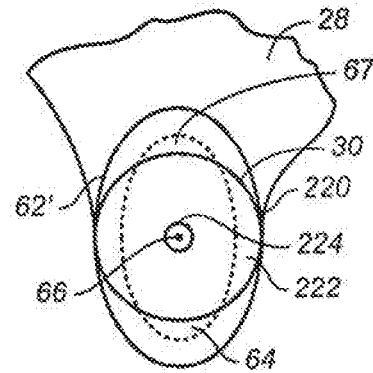


FIG. 12B

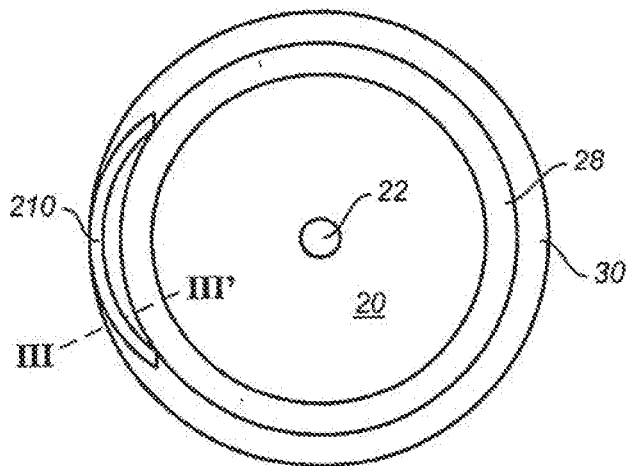


FIG. 12C

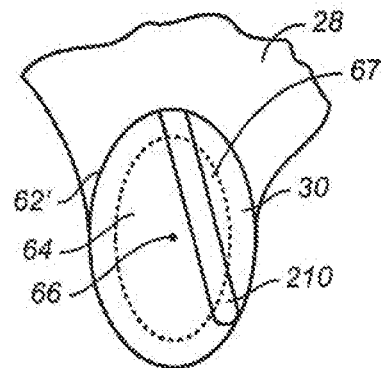


FIG. 12D

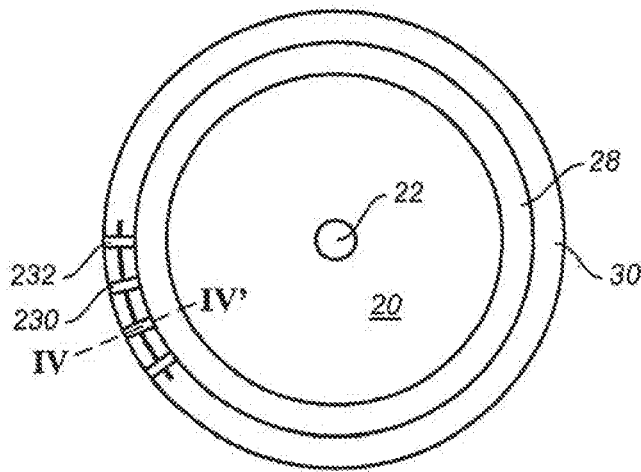


FIG. 12E

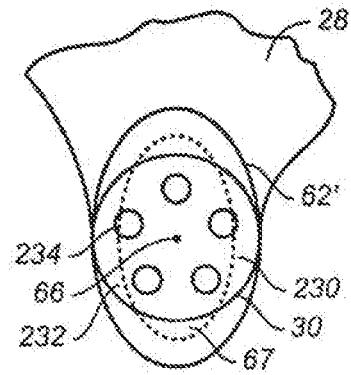


FIG. 12F

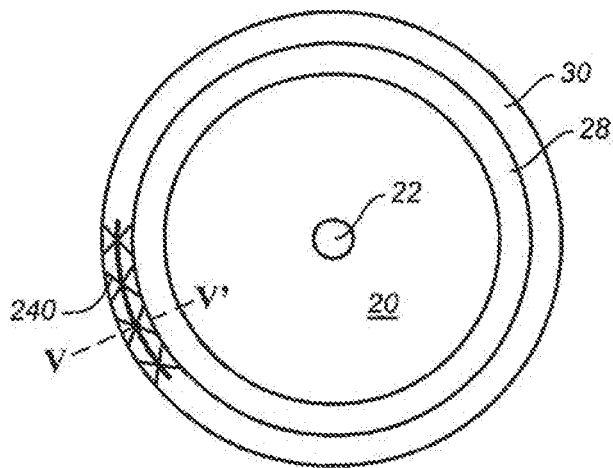


FIG. 12G

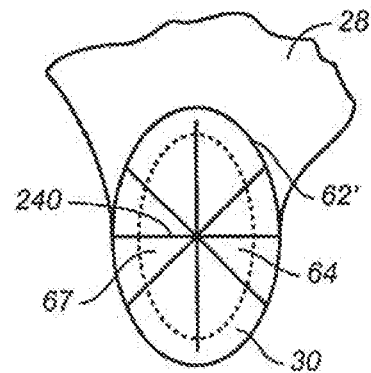
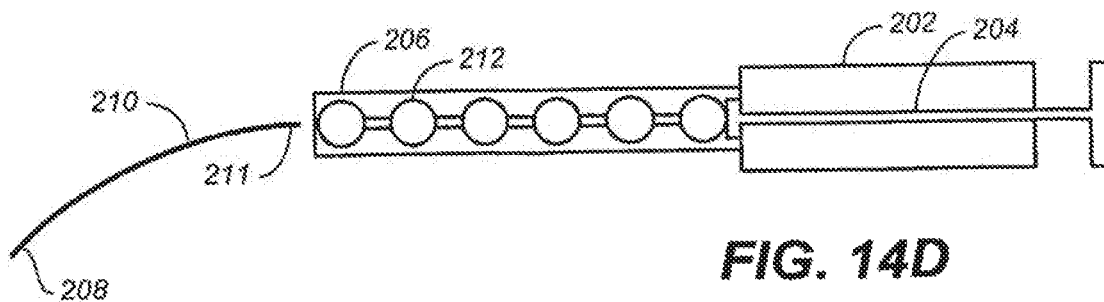
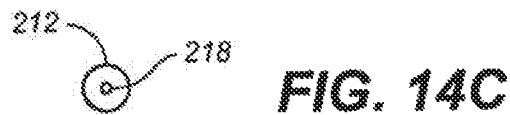
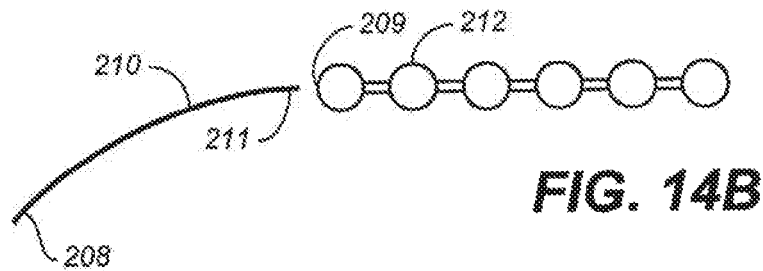
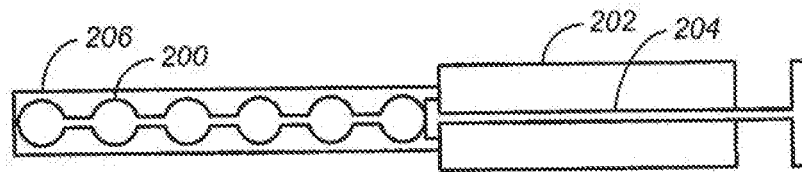
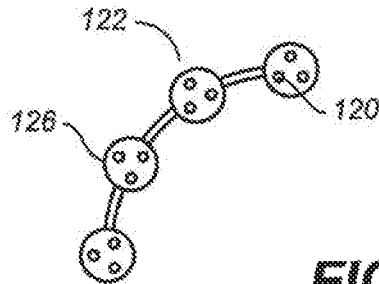


FIG. 12H



US 11,389,328 B2

1

INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 15/182,165, filed Jun. 14, 2016, now issued as U.S. Pat. No. 10,314,742, which is a continuation of U.S. patent application Ser. No. 13/025,112, filed Feb. 10, 2011, now issued as U.S. Pat. No. 9,370,443, which is a divisional of U.S. patent application Ser. No. 11/475,523, filed Jun. 26, 2006, now issued as U.S. Pat. No. 7,909,789, each of which is hereby incorporated by reference in its entirety.

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of

2

surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjunctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmur flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's

US 11,389,328 B2

3

canal. The support does not substantially interfere with transmur flow across Schlemm's canal, and thereby utilizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocompatible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer; a polyorthoester; a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a poly-anhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted

4

between three beads, the connectors may be of the same or different lengths. The connectors can include the same or different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmur flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmur flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can

US 11,389,328 B2

5

include implanting at least two supports. If more than one support is implanted within a single eye, the multiple supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 provides a partial cross-sectional side view of a normal human eye.

FIG. 2 provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. 3 shows a front view of normal fluid drainage from the eye.

FIG. 4A shows an alternative front view of normal fluid drainage paths from the eye. FIG. 4B shows a cross-sectional view along line I-I'.

FIG. 5A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. 5B shows a front view of a device including a support inserted into Schlemm's canal that allows transmurial flow across the canal. FIG. 5C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmurial flow across the canal.

FIG. 6A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. 6B shows the corresponding front views of the element or bead configurations shown in FIG. 6A. FIG. 6C illustrates an element or bead having fenestrations.

FIG. 7A illustrates a support having multiple juxtaposed beads. FIG. 7B illustrates a support having multiple juxtaposed and connected beads. FIG. 7C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. 7D shows a support having multiple, spaced-apart but connected beads. FIG. 7E illustrates beads threaded onto a connector.

FIGS. 8A-B show side and front views, respectively, of a support having an open network structure. FIGS. 8C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at least three points (labeled P₁, P₂, P₃). FIGS. 8E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. 8G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. 9A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. 10A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. 11A-B and D illustrate configurations of supports having a smaller radius of curvature than Schlemm's canal. FIG. 11C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. 12A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. 12B

6

shows a cross-sectional view along line II-II'. FIG. 12C illustrates a variation of a support traversing the central core of the canal. FIG. 12D shows a cross-sectional view along line III-III'. FIG. 12E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. 12F shows a cross-sectional view along line IV-IV'. FIG. 12G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. 12H shows a cross-sectional view along line V-V'.

FIG. 13 shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. 14A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. 14B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. 14C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. 14D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmural fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. 1 shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body 12 is connected to iris 18 and to lens 16 via zonular fibrils 14. The anterior chamber of the eye 20 is bounded on its anterior (front) surface by cornea 24. In the center of iris 18 is pupil 22. Cornea 24 is connected on its periphery to sclera 26, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork 28 is located on the outer peripheral surface of anterior chamber 20. The trabecular meshwork extends 360° circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork 28 is Schlemm's canal 30. Schlemm's canal extends 360° circumferentially around the trabecular meshwork. At the apex formed between iris 18, meshwork 28 and sclera 26 is angle 32. Conjunctiva 34 is a membrane overlaying sclera 26 and lining the inside of the eyelid (not shown).

FIG. 2 shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body 12 and its path through and out of the eye is indicated by solid directional line 36. The aqueous humor flows from ciliary body 12, between lens 16 and iris 18, through pupil 22 into anterior chamber 20, across trabecular meshwork 28, across Schlemm's canal 30, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. 3 shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber 20 via pupil 22. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines 36. The fluid crosses trabecular meshwork 28 and traverses Schlemm's canal 30 to reach aqueous veins or collector channels 38. There are typically 25-30 collector channels located in a human eye. Collector

US 11,389,328 B2

7

channels **38** are connected to vasculature **40**, whereby the drained aqueous humor enters the bloodstream. Although the direction of net or bulk fluid flow is depicted as radially outward by directional lines **36** from pupil **22** for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. 4A-B. FIG. 4A shows a front view of an eye, and FIG. 4B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal **30** is depicted by directional lines **50**. Fluid that does not traverse canal **30** to reach collector channels **38** may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines **52**, **52'**, and **52''**. In each of these paths, fluid enters trabecular meshwork **28** along its inner peripheral surface **60** and exits the meshwork along its outer peripheral surface **62'**. Meshwork outer peripheral surface **62'** provides the inner peripheral surface or wall of Schlemm's canal **30**. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork **38** through inner peripheral surface or wall **62'** of Schlemm's canal **30** to reach lumen **64** of the canal. Second, fluid must flow from lumen **64** through canal outer peripheral wall **62''** through apertures **38'** to enter collector channels **38**. Finally, the collector channels **38** feed the drained fluid into vasculature. Lumen **64** of canal **30** includes a central core region **67**. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion of the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflow from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1)

8

fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral boundary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the collector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. 5A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal **30**, where canal outer peripheral wall **62''** is very close to canal inner peripheral wall **62'**. Although Schlemm's canal **30** is depicted in FIG. 5A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels **38** is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. 5B illustrates an example of a device **70** inserted into Schlemm's canal **30** through incision site **74**. Device **70** in this example is positioned to one side of incision site **74**. Device **70** includes support **72** that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall **62'** and canal outer wall **62''** to reach collector channels **38** via apertures **38'**. In the example shown in FIG. 5B, support **72** includes elements or beads **76** connected with connectors **78**. In this variation, the distance between canal inner wall **62'** and outer wall **62''** is approximately determined by the cross-sectional dimension of support **72**, which is in turn determined by the largest cross-sectional diameter of the beads **76**. Therefore, circum-

US 11,389,328 B2

9

ferential (i.e., longitudinal) fluid flow around and along the canal **30** indicated by directional line **50** may be inhibited by the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52''** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters (e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. 5C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. 5B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. 6A and 6B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. 6C, elements or beads **76** may include fenestrations **99**, **99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. 6C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. 7A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. 7A), connected and juxtaposed (FIGS. 7B and 7C), or connected together with connectors **100**, **100'** to form intervals between beads (FIG. 7D). In addition, beads may be threaded onto a connector **101** (FIG. 7E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. 7B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. 7C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide

10

wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knotting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. 7D, multiple connectors **100**, **100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100**, **100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100**, **100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. 7E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100**, **100'**, **101** can be flexible, such as thin polymer threads or metal wires. Connectors **100**, **100'**, **101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100**, **100'**, **101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. 8A-F. As illustrated in FIG. 8A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. 8A-B will have minimal surface area contact with the walls of Schlemm's canal. i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. 8C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. 8C, the support will contact the wall of Schlemm's canal at at least three points, labeled P_1 , P_2 , and P_3 , after implantation. In FIGS. 8E-H, examples of rod-like supports having fluted edges are shown. In FIGS. 8E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include

US 11,389,328 B2

11

fenestrations **113**. The support can include central bore **117**. In FIGS. **8G-H**, fluted edges **110'** extend along sides **112'** to form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. **8E-H**, the support may contact the canal walls at at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. **8A-B** shows, some supports only have point contacts with the canal wall. For the supports shown in FIGS. **5B-C**, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. **6A-B** may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. **7D-E** that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. **8C-D**, in some variations, the support contacts the interior wall of the canal at at least two points; or at at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided FIGS. **9A-B**. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder **C** having length **L**, extending circumferentially from a first end **X₁** to a second end **X₂** of support **152**, and inside radius **R_i**. In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder **C** as described above. In other variations, the support contacts less than 10% of the surface area of **C**. In still other variations, the support contacts less than 30% of the surface area of **C**. For example, the support **152** shown in FIGS. **9A-B** contacts the canal wall **62** only at bead outer peripheral edges at **E₁-E₇**, along a distance of the bead width **B_w**. There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmural flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapeable metal having a sinusoidal or zig-zag configuration as shown FIGS. **8C-D**, a cross-sectional dimension **117** of the support can be decreased or increased by apply tension along dimension **119**. As illustrated in FIG. **10A**, a support **160** can extend

12

essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately half way around the circumference of the canal (not shown). As shown in FIG. **10B**, a support **162** can extend less than halfway around the canal. As shown in FIG. **10C**, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. **11A**, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension **B_D**. Support **132** comprises a stiff arcuate element **135** with a radius of curvature **R_{supp}** smaller than the radius of curvature of Schlemm's canal **R_{SC}**. The smaller, fixed radius of curvature **R_{supp}** of arcuate member **135** urges canal **30** to open more than **B_D**. In other variations shown in FIGS. **11B** and **11D**, support **179** comprises an arcuate member **180** without beads having a radius of curvature **R_{supp}** that is less than the radius of curvature **R_{SC}** of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. **11C**, support **181** comprises an arcuate member **182** having a radius of curvature **R_{supp}** larger than that of Schlemm's canal **R_{SC}**. Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. **11C**, support **181** can include beads **184**. To urge open the canal, the radius of curvature **R_{supp}** of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal **R_{SC}**. For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member **R_{supp}** in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature **R_{supp}** of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at at least one point. Referring to FIG. **12A**, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. **12B** shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. **12C**, a front view of an arcuate support **210** is shown. FIG. **12D** shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. **12E**, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. **12F**. As illustrated

US 11,389,328 B2

13

in FIG. 12F, bead 232 with fenestrations 234 occupies the majority of central core 67 of canal 30. In other variations, the support occupies only a small portion of the central core of the canal. For example, in FIG. 12G, a front view of a support 240 having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. 12H.

A support can be made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacrylate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives, flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly(lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly(ethylene glycol) copolymer, a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer, a poly(lactic acid)/poly(ethylene glycol) copolymer, a poly(glycolic acid)/poly(ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone)/poly(ethylene glycol) copolymer, a polyorthoester, a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a polyanhydride, a poly(dioxanone), a poly(alkylene alkylate), a copolymer of polyethylene glycol and a polyorthoester, a biodegradable polyurethane, a poly(amino acid), a polyetherester, a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(e-caprolactone) dimethacrylate and n-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable

14

method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. 13, predetermined localized portions 120 of support 122 can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions 120 will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads 126 in support 120 are hollow, then after irradiation and ablation, features 120 will become fenestrations. The fenestrations can be created to make support 122 more porous in nature or to allow release of an active agent from within a support. e.g., from within beads 126. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example.

US 11,389,328 B2

15

Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminescent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the support may be allowed to self-position in Schlemm's canal. In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

16

FIGS. 14A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. 14A, a support 200 can be introduced into the canal using syringe 202 and plunger 204. Syringe 202 has distal end 206 that can be at least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger 204, thereby pushing support 200 into the canal. Referring to FIGS. 14B-C, distal end 208 of guide element 210 can be at least partially introduced into the canal. Guide element 210 can be a guide wire. Guide element 210 can be extended circumferentially along the canal to aid in positioning the support. Support 212 comprises central bore 218 capable of accommodating guide element 210 such that support 212 can be threaded onto guide element 210 and slidably positioned along the guide element. Once distal end 209 of support 212 is threaded onto guide element 210, support 212 can be pushed in a distal direction along guide element 210 to insert support 212 into the canal. In some variations, support 212 can remain threaded onto guide element 210, and guide element 210 can remain in the canal. In other variations, support 212 can be slid off distal end 208 of guide element 210, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. 14C-D, syringe 202 with plunger 204 can be used in combination with a guide element 210. In this variation, distal end 208 of guide element 210 is inserted at least partially into Schlemm's canal. Guide element 210 can be extended circumferentially along the canal to aid in positioning the support. Support 212 has central bore 218 capable of accommodating guide element 210. Proximal end 211 of guide element 210 is inserted into bore 218. Plunger 204 is depressed in a distal direction to push support 212 into the canal and slide support 212 along element 210. Guide element 210 can remain in the canal or be removed following insertion of the support. Supports 200, 212 must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as

US 11,389,328 B2

17

mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more mirrors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmurial flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the

18

circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. 11A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

The invention claimed is:

1. A method for reducing intraocular pressure in a patient using a support and an introducer comprising a cannula, comprising:

positioning a distal end of the cannula at or near Schlemm's canal, wherein the support is located in a lumen of the cannula; and

pushing the support distally out of the distal end of the cannula to insert the support circumferentially within Schlemm's canal,

wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal such that at least a portion of the arcuate member extends out of Schlemm's canal.

2. The method of claim 1, wherein the patient has glaucoma.

3. The method of claim 1, further comprising anchoring the support to tissue surrounding Schlemm's canal.

4. The method of claim 1, further comprising dilating Schlemm's canal prior to inserting the support.

5. The method of claim 4, wherein Schlemm's canal is dilated by injecting fluid into the canal.

6. The method of claim 1, wherein the support at least partially props open Schlemm's canal.

7. The method of claim 1, wherein the support does not significantly block fluid outflow to the collector channels after insertion into Schlemm's canal.

US 11,389,328 B2

19

8. The method of claim 1, wherein the support does not significantly block fluid outflow from the trabecular meshwork after insertion into Schlemm's canal.

9. The method of claim 1, wherein R_{supp} is about 10% smaller than the radius of curvature of Schlemm's canal.

10. The method of claim 1, wherein R_{supp} is about 20% smaller than the radius of curvature of Schlemm's canal.

11. The method of claim 1, wherein R_{supp} is about 30% smaller than the radius of curvature of Schlemm's canal.

12. The method of claim 1, wherein R_{supp} is about 40% smaller than the radius of curvature of Schlemm's canal.

13. The method of claim 1, wherein R_{supp} is about 50% smaller than the radius of curvature of Schlemm's canal.

14. The method of claim 1, wherein R_{supp} is about 3 mm.

15. The method of claim 1, wherein R_{supp} is about 4 mm.

16. The method of claim 1, wherein R_{supp} is about 5 mm.

17. The method of claim 1, wherein the support extends less than a quarter of the way around Schlemm's canal after insertion into the canal.

18. The method of claim 1, wherein the support extends about one quarter of the way around Schlemm's canal after insertion into the canal.

20

19. The method of claim 1, wherein the support extends about one half of the way around Schlemm's canal after insertion into the canal.

20. The method of claim 1, wherein the support extends about all the way around Schlemm's canal after insertion into the canal.

21. The method of claim 1, wherein when the support is inserted within a cylindrical section of the lumen of Schlemm's canal having an internal wall surface area C, the support contacts less than 30% of the surface area of C.

22. The method of claim 1, wherein the support comprises at least one fenestration.

23. The method of claim 1, wherein the support comprises a plurality of fenestrations.

24. The method of claim 1, wherein the support is non-tubular.

25. The method of claim 1, wherein the support comprises a shape memory alloy.

26. The method of claim 1, wherein the support has a first shape prior to insertion within Schlemm's canal and a second shape after insertion.

27. The method of claim 1, wherein the support has a sinusoidal shape.

* * * * *

EXHIBIT F

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
22 June 2017 (22.06.2017)



(10) International Publication Number
WO 2017/106517 A1

(51) International Patent Classification:

A61F 2/16 (2006.01) A61F 9/007 (2006.01)
A61M 5/00 (2006.01) A61M 25/00 (2006.01)
A61F 9/00 (2006.01) A61M 1/00 (2006.01)

(21) International Application Number:

PCT/US2016/066957

(22) International Filing Date:

15 December 2016 (15.12.2016)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/267,794 15 December 2015 (15.12.2015) US

(71) Applicant: **IVANTIS, INC.** [US/US]; 38 Discovery, Suite 150, Irvine, CA 92618 (US).

(72) Inventors: **SCHIEBER, Andrew, T.**; 38 Discovery, Suite 150, Irvine, CA 92618 (US). **EUTENEUER, Charles, L.**; 38 Discovery, Suite 150, Irvine, CA 92618 (US). **VAN METER, David, T.**; 38 Discovery, Suite 150, Irvine, CA 92618 (US). **GALT, Kenneth, M.**; 38 Discovery, Suite 150, Irvine, CA 92618 (US).

(74) Agents: **THOMAS, Justin** et al.; Shay Glenn LLP, 2755 Campus Drive, Suite 210, San Mateo, CA 94403 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: OCULAR IMPLANT AND DELIVERY SYSTEM

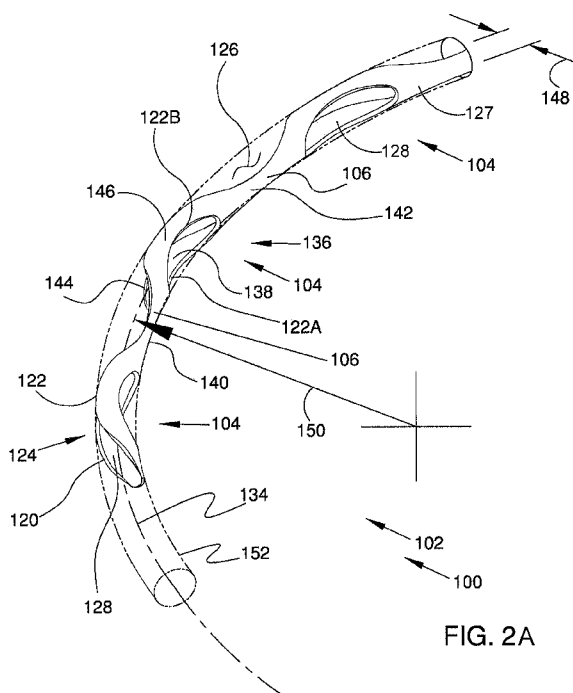


FIG. 2A

(57) Abstract: An illustrative method for reducing intraocular pressure in a patient may comprise deploying an ocular implant adapted to reside at least partially in a portion of Schlemm's canal of an eye and administering a therapeutic agent comprising a Rho kinase (ROCK) inhibitor to the patient. The ocular implant may be configured to lower the intraocular pressure from an initial to a second pressure within a first range and the therapeutic agent may lower an intraocular pressure to a third pressure within a second range, the third pressure lower than the second pressure.

WO 2017/106517 A1

WO 2017/106517 A1



Published:

— with international search report (Art. 21(3))

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

OCULAR IMPLANT AND DELIVERY SYSTEM

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit under 35 U.S.C. § 119 of US Patent Appl. No. 62/267,794
5 filed December 15, 2015, the disclosure of which is incorporated by reference.

INCORPORATION BY REFERENCE

[0002] All publications and patent applications mentioned in this specification are herein
incorporated by reference to the same extent as if each individual publication or patent application was
10 specifically and individually indicated to be incorporated by reference.

TECHNICAL FIELD

[0003] The present disclosure pertains generally, but not by way of limitation, to medical devices,
and methods for manufacturing medical devices. The present invention relates generally to devices that
15 are implanted within the eye. More particularly, the present invention relates to devices that facilitate the
transfer of fluid from within one area of the eye to another area of the eye. Additionally, the present
disclosure relates to systems, devices and methods for delivering ocular implants into the eye.

BACKGROUND

20 [0004] According to a draft report by The National Eye Institute (NEI) at The United States National
Institutes of Health (NIH), glaucoma is now the leading cause of irreversible blindness worldwide and the
second leading cause of blindness, behind cataract, in the world. Thus, the NEI draft report concludes, “it
is critical that significant emphasis and resources continue to be devoted to determining the
pathophysiology and management of this disease.” Glaucoma researchers have found a strong correlation
25 between high intraocular pressure and glaucoma. For this reason, eye care professionals routinely screen
patients for glaucoma by measuring intraocular pressure using a device known as a tonometer. Many
modern tonometers make this measurement by blowing a sudden puff of air against the outer surface of
the eye.

[0005] The eye can be conceptualized as a ball filled with fluid. There are two types of fluid inside
30 the eye. The cavity behind the lens is filled with a viscous fluid known as vitreous humor. The cavities in
front of the lens are filled with a fluid known as aqueous humor. Whenever a person views an object, he or
she is viewing that object through both the vitreous humor and the aqueous humor.

[0006] Whenever a person views an object, he or she is also viewing that object through the cornea
and the lens of the eye. In order to be transparent, the cornea and the lens can include no blood vessels.
35 Accordingly, no blood flows through the cornea and the lens to provide nutrition to these tissues and to
remove wastes from these tissues. Instead, these functions are performed by the aqueous humor. A
continuous flow of aqueous humor through the eye provides nutrition to portions of the eye (e.g., the

WO 2017/106517

PCT/US2016/066957

cornea and the lens) that have no blood vessels. This flow of aqueous humor also removes waste from these tissues.

[0007] Aqueous humor is produced by an organ known as the ciliary body. The ciliary body includes epithelial cells that continuously secrete aqueous humor. In a healthy eye, a stream of aqueous humor flows out of the anterior chamber of the eye through the trabecular meshwork and into Schlemm's canal as new aqueous humor is secreted by the epithelial cells of the ciliary body. This excess aqueous humor enters the venous blood stream from Schlemm's canal and is carried along with the venous blood leaving the eye.

[0008] When the natural drainage mechanisms of the eye stop functioning properly, the pressure inside the eye begins to rise. Researchers have theorized prolonged exposure to high intraocular pressure causes damage to the optic nerve that transmits sensory information from the eye to the brain. This damage to the optic nerve results in loss of peripheral vision. As glaucoma progresses, more and more of the visual field is lost until the patient is completely blind.

[0009] In addition to drug treatments, a variety of surgical treatments for glaucoma have been performed. For example, shunts were implanted to direct aqueous humor from the anterior chamber to the extraocular vein (Lee and Scheppens, "Aqueous-venous shunt and intraocular pressure," Investigative Ophthalmology (February 1966)). Other early glaucoma treatment implants led from the anterior chamber to a sub-conjunctival bleb (e.g., U.S. Pat. No. 4,968,296 and U.S. Pat. No. 5,180,362). Still others were shunts leading from the anterior chamber to a point just inside Schlemm's canal (Spiegel et al., "Schlemm's canal implant: a new method to lower intraocular pressure in patients with POAG?" Ophthalmic Surgery and Lasers (June 1999); U.S. Pat. No. 6,450,984; U.S. Pat. No. 6,450,984).

SUMMARY

[0010] The invention provides design, material, and manufacturing method alternatives for medical devices.

[0011] An illustrative method for reducing intraocular pressure in a patient may comprise deploying an ocular implant adapted to reside at least partially in a portion of Schlemm's canal of an eye and administering a therapeutic agent comprising a Rho kinase (ROCK) inhibitor to the patient. The implant may comprise a tubular body having an inner surface and an outer surface. The tubular body may extend in a curved volume whose longitudinal axis forms an arc of a circle. A plurality of open areas and strut areas may be formed in the tubular body and the strut areas may surround the plurality of open areas. The tubular body may have a diameter of between 0.005 inches and 0.04 inches. The ocular implant may be configured to lower the intraocular pressure from an initial to a second pressure within a first range and the therapeutic agent may lower an intraocular pressure to a third pressure within a second range, the third pressure lower than the second pressure.

[0012] In another illustrative embodiment a kit for reducing intraocular pressure in a patient may be provided. The kit may comprise an ocular implant adapted to reside at least partially in a portion of Schlemm's canal of an eye, a cannula defining a passageway extending from a proximal end to a distal

WO 2017/106517

PCT/US2016/066957

end, a delivery tool having a distal interlocking portion engaging a complementary interlocking portion of the ocular implant, and a therapeutic agent comprising a Rho kinase (ROCK) inhibitor. The cannula may have a distal opening extending through a side wall and the distal end of the cannula to form a trough, a curved distal portion, a curved intermediate portion, and a proximal portion.

5 **[0013]** The above summary of some examples and embodiments is not intended to describe each disclosed embodiment or every implementation of the present disclosure. The Brief Description of the Drawings, and Detailed Description, which follow, more particularly exemplify these embodiments, but are also intended as exemplary and not limiting.

10 **[0014]** In one embodiment, a method for reducing intraocular pressure in a patient is provided, the method comprising deploying an ocular implant adapted to reside at least partially in a portion of Schlemm's canal of an eye, the implant comprising, a tubular body having an inner surface and an outer surface, the tubular body extending in a curved volume whose longitudinal axis forms an arc of a circle, and a plurality of open areas and strut areas formed in the tubular body, the strut areas surrounding the plurality of open areas, and the tubular body having a diameter of between 0.005 inches and 0.04 inches, 15 wherein the ocular implant is configured to lower the intraocular pressure from an initial to a second pressure within a first range, and administering a therapeutic agent comprising a Rho kinase (ROCK) inhibitor to the patient to lower an intraocular pressure to a third pressure within a second range, the third pressure lower than the second pressure.

20 **[0015]** In some embodiments, deploying the ocular implant comprises inserting a distal end of a cannula through an incision in the eye and into an anterior chamber of the eye, placing the distal opening of the cannula into fluid communication with Schlemm's canal such that the cannula enters Schlemm's canal in a substantially tangential orientation, advancing the ocular implant distally through the cannula with a delivery tool engaged with the ocular implant, a proximal portion of the ocular implant engaging the delivery tool proximal to a distal portion of the delivery tool, and disengaging the ocular implant and 25 the delivery tool when the proximal portion of the ocular implant reaches distal opening of the cannula.

30 **[0016]** In some embodiments, the first range is approximately 20 to 30 mm Hg. In other embodiments, the first range is approximately 23 to 28 mm Hg. In other embodiments, the second range is approximately 13 to 23 mm Hg. In some embodiments, the second range is approximately 15 to 20 mm Hg.

35 **[0017]** In one embodiment, the implant further comprises a first pressure sensor disposed on the inner surface of the tubular body.

40 **[0018]** A method for reducing intraocular pressure in a patient is also provided, the method comprising, deploying an ocular implant adapted to reside at least partially in a portion of Schlemm's canal of an eye, the implant comprising a tubular body having an inner surface and an outer surface, the tubular body extending in a curved volume whose longitudinal axis forms an arc of a circle, and a plurality of open areas and strut areas formed in the tubular body, the strut areas surrounding the plurality of open areas, and the tubular body having a diameter of between 0.005 inches and 0.04 inches, wherein the ocular implant is configured to lower the intraocular pressure to a second pressure less than the initial

WO 2017/106517

PCT/US2016/066957

pressure, and administering a therapeutic agent comprising a Rho kinase (ROCK) inhibitor to the patient to lower an intraocular pressure from an initial to a third pressure, the third pressure less than the second pressure.

5 [0019] In one embodiment, deploying the ocular implant comprises inserting a distal end of a cannula through an incision in the eye and into an anterior chamber of the eye, placing the distal opening of the cannula into fluid communication with Schlemm's canal such that the cannula enters Schlemm's canal in a substantially tangential orientation, advancing the ocular implant distally through the cannula with a delivery tool engaged with the ocular implant, a proximal portion of the ocular implant engaging the delivery tool proximal to a distal portion of the delivery tool, and disengaging the ocular implant and
10 the delivery tool when the proximal portion of the ocular implant reaches distal opening of the cannula.

[0020] In some embodiments, the second pressure is approximately 65 to 95% of the initial pressure. In another embodiment, the second pressure is approximately 75 to 85% of the initial pressure.

[0021] In one embodiment, the third pressure is approximately 65 to 95% of the second pressure. In another embodiment, the third pressure is approximately 75 to 85% of the second pressure.

15 [0022] In some embodiments, the implant further comprises a first pressure sensor disposed on the inner surface of the tubular body.

[0023] A kit for reducing intraocular pressure in a patient is provided, the kit comprising, an ocular implant adapted to reside at least partially in a portion of Schlemm's canal of an eye, a cannula defining a passageway extending from a proximal end to a distal end, the cannula having a distal opening extending
20 through a side wall and the distal end of the cannula to form a trough, a curved distal portion, a curved intermediate portion, and a proximal portion, and a delivery tool having a distal interlocking portion engaging a complementary interlocking portion of the ocular implant, a therapeutic agent comprising a Rho kinase (ROCK) inhibitor.

[0024] In one embodiment, the kit further comprises a therapeutic agent delivery device.

25 [0025] In another embodiment, the therapeutic agent delivery device comprises an eye dropper.

[0026] In some embodiments, the ocular implant comprises a tubular body having an inner surface and an outer surface, the tubular body extending in a curved volume whose longitudinal axis forms an arc of a circle, and a plurality of open areas and strut areas formed in the tubular body, the strut areas surrounding the plurality of open areas, and the tubular body having a diameter of between 0.005 inches
30 and 0.04 inches.

[0027] In one embodiment, the ocular implant further comprises a first pressure sensor disposed on the inner surface of the tubular body.

[0028] In another embodiment, the therapeutic agent is disposed on a surface of the ocular implant.

WO 2017/106517

PCT/US2016/066957

BRIEF DESCRIPTION OF THE DRAWINGS

[0029] The disclosure may be more completely understood in consideration of the following detailed description of various embodiments in connection with the accompanying drawings, in which:

[0030] Figure 1 is a stylized perspective view depicting a portion of a human eye and a portion of an ocular implant disposed in Schlemm's canal.

[0031] Figure 2A is an enlarged perspective view showing a portion of the implant of Figure 1.

[0032] Figure 2B is another enlarged perspective view showing a portion of the implant of Figure 1 including a coating.

[0033] Figure 3 is a perspective view showing a volume defined by the body of the ocular implant of Figures 1 and 2.

[0034] Figure 4 is a perspective view showing a first plane intersecting the body of an ocular implant.

[0035] Figure 5 is a perspective view showing a bending moment being applied to an ocular implant.

[0036] Figure 6 is a plan view of the implant shown in Figure 5 but in the absence of any bending moment.

[0037] Figure 7A is a lateral cross-sectional view of the ocular implant of Figure 6 taken along section line A-A of Figure 6.

[0038] Figure 7B is a lateral cross-sectional view of the ocular implant of Figure 6 taken along section line B-B of Figure 6.

[0039] Figure 8 is an enlarged cross-sectional view of the ocular implant of Figure 6 taken along section line B-B of Figure 6.

[0040] Figure 9 is an enlarged cross-sectional view of the ocular implant of Figure 6 taken along section line A-A of Figure 6.

[0041] Figure 10A is an enlarged perspective view of a portion of the ocular implant including a pressure sensor.

[0042] Figure 10B is a cross-sectional view of the illustrative pressure sensor of Figure 10A, taken at line B-B.

[0043] Figure 10C is an enlarged perspective view of another portion of the ocular implant including a pressure sensor.

[0044] Figure 11 is a stylized view of an electronic device receiving data from an implanted ocular implant.

[0045] Figure 12 is a plan view showing an ocular implant according to another embodiment of the invention having a longitudinal radius of curvature that varies along its length.

[0046] Figure 13 is a perspective view showing an ocular implant according to yet another embodiment of the invention that has substantially no radius of curvature.

[0047] Figure 14 is a stylized representation of a medical procedure in accordance with this DETAILED DESCRIPTION.

WO 2017/106517

PCT/US2016/066957

[0048] Figure 15 is an enlarged perspective view further illustrating the delivery system and the eye shown in Figure 14.

[0049] Figure 16A is a perspective view showing a delivery system including an ocular implant and a cannula defining a passageway that is dimensioned to slidably receive the ocular implant.

5 **[0050]** Figure 16B is an enlarged detail view further illustrating the ocular implant and the cannula 108 shown in FIG. 6A.

[0051] Figure 17 is a perspective view of a cannula in accordance with the detailed description.

[0052] Figure 18 is a perspective view of an assembly including the cannula shown in Figure 17 and an ocular implant that is resting in a passageway defined by the cannula.

10 **[0053]** Figure 19 is a stylized perspective view including the assembly shown in Figure 18.

[0054] Figure 20 is an enlarged perspective view showing a portion of the cannula shown in the assembly of Figure 19.

[0055] Figure 21 is an additional perspective view showing the ocular implant and the cannula shown in the previous Figure 20.

15 **[0056]** Figure 22 is an additional perspective view showing the ocular implant and the cannula shown in Figure 21.

[0057] Figure 23 is an additional perspective view showing the ocular implant and the cannula shown in Figures 21 and 22.

20 **[0058]** Figure 24 is a perspective view of Schlemm's canal after the cannula shown in Figure 23 has been withdrawn leaving an inlet portion of the ocular implant in the anterior chamber of the eye and the remainder of ocular implant in Schlemm's canal.

[0059] Figure 25A is a perspective view showing another illustrative delivery system including an ocular implant and a cannula defining a passageway that is dimensioned to slidably receive the ocular implant.

25 **[0060]** Figure 25B is an enlarged detail view further illustrating the ocular implant and the cannula shown in Figure 25A.

[0061] Figure 26 is an enlarged perspective view further illustrating the delivery system shown in Figure 25 and an eye.

[0062] Figure 27 is a perspective view further illustrating delivery system shown in Figure 25.

30 **[0063]** Figure 28 is a side view further illustrating the cannula shown in Figure 25.

[0064] Figure 28A is an additional side view illustrating the cannula shown in Figure 25.

[0065] Figure 29 is an enlarged detail view further illustrating the cannula shown in Figure 25.

[0066] Figure 30 is an enlarged perspective view further illustrating the distal portion of the cannula shown in Figure 25.

35 **[0067]** Figure 31 is a schematic view of an illustrative kit for reducing intraocular pressure in a patient.

WO 2017/106517

PCT/US2016/066957

[0068] While the disclosure is amenable to various modifications and alternative forms, specifics thereof have been shown by way of example in the drawings and will be described in detail. It should be understood, however, that the intention is not to limit the invention to the particular embodiments described. On the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the disclosure.

DETAILED DESCRIPTION

[0069] The following description should be read with reference to the drawings, which are not necessarily to scale, wherein like reference numerals indicate like elements throughout the several views.

10 The detailed description and drawings are intended to illustrate but not limit the claimed invention. Those skilled in the art will recognize that the various elements described and/or shown may be arranged in various combinations and configurations without departing from the scope of the disclosure. The detailed description and drawings illustrate example embodiments of the claimed invention.

[0070] Definitions of certain terms are provided below and shall be applied, unless a different definition is given in the claims or elsewhere in this specification.

[0071] All numeric values are herein assumed to be modified by the term “about,” whether or not explicitly indicated. The term “about” generally refers to a range of numbers that one of skill in the art would consider equivalent to the recited value (i.e., having the same or substantially the same function or result). In many instances, the terms “about” may include numbers that are rounded to the nearest significant figure. Other uses of the term “about” (i.e., in a context other than numeric values) may be assumed to have their ordinary and customary definition(s), as understood from and consistent with the context of the specification, unless otherwise specified.

[0072] The recitation of numerical ranges by endpoints includes all numbers within that range (e.g., 1 to 5 includes 1, 1.5, 2, 2.75, 3, 3.80, 4, and 5).

25 [0073] As used in this specification and the appended claims, the singular forms “a,” “an,” and “the” include or otherwise refer to singular as well as plural referents, unless the content clearly dictates otherwise. As used in this specification and the appended claims, the term “or” is generally employed to include “and/or,” unless the content clearly dictates otherwise.

WO 2017/106517

PCT/US2016/066957

[0074] It is noted that references in the specification to "an embodiment", "some embodiments", "other embodiments", etc., indicate that the embodiment(s) described may include a particular feature, structure, or characteristic, but every embodiment may not necessarily include the particular feature, structure, or characteristic. Moreover, such phrases are not necessarily referring to the same embodiment.

5 Further, when a particular feature, structure, or characteristic is described in connection with an embodiment, it would be within the knowledge of one skilled in the art to affect such feature, structure, or characteristic in connection with other embodiments, whether or not explicitly described, unless clearly stated to the contrary. That is, the various individual elements described below, even if not explicitly shown in a particular combination, are nevertheless contemplated as being combinable or able to be
10 arranged with each other to form other additional embodiments or to complement and/or enrich the described embodiment(s), as would be understood by one of ordinary skill in the art.

[0075] The following detailed description should be read with reference to the drawings, in which similar elements in different drawings are identified with the same reference numbers. The drawings, which are not necessarily to scale, depict illustrative embodiments and are not intended to limit the scope
15 of the disclosure.

[0076] Figure 1 is a stylized perspective view depicting a portion of a human eye 20. Eye 20 can be conceptualized as a fluid filled ball having two chambers. Sclera 22 of eye 20 surrounds a posterior chamber 24 filled with a viscous fluid known as vitreous humor. Cornea 26 of eye 20 encloses an anterior chamber 30 that is filled with a fluid known as aqueous humor. The cornea 26 meets the sclera 22
20 at a limbus 28 of eye 20. A lens 32 of eye 20 is located between anterior chamber 30 and posterior chamber 24. Lens 32 is held in place by a number of ciliary zonules 34. Whenever a person views an object, he or she is viewing that object through the cornea, the aqueous humor, and the lens of the eye. In order to be transparent, the cornea and the lens can include no blood vessels. Accordingly, no blood flows through the cornea and the lens to provide nutrition to these tissues and to remove wastes from
25 these tissues. Instead, these functions are performed by the aqueous humor. A continuous flow of aqueous humor through the eye provides nutrition to portions of the eye (e.g., the cornea and the lens) that have no blood vessels. This flow of aqueous humor also removes waste from these tissues.

[0077] Aqueous humor is produced by an organ known as the ciliary body. The ciliary body includes epithelial cells that continuously secrete aqueous humor. In a healthy eye, a stream of aqueous
30 humor flows out of the eye as new aqueous humor is secreted by the epithelial cells of the ciliary body. This excess aqueous humor enters the blood stream and is carried away by venous blood leaving the eye.

[0078] In a healthy eye, aqueous humor flows out of the anterior chamber 30 through the trabecular meshwork 36 and into Schlemm's canal 38, located at the outer edge of the iris 42. Aqueous humor exits Schlemm's canal 38 by flowing through a number of outlets 40. After leaving Schlemm's canal 38,
35 aqueous humor is absorbed into the venous blood stream.

[0079] In Figure 1, an ocular implant 100 is disposed in Schlemm's canal 38 of eye 20. Ocular implant 100 has a body 102 including a plurality of tissue supporting frames 104 and a plurality of spines 106. Body 102 also includes a first edge 120 and a second edge 122 that define a first opening 124. First

WO 2017/106517

PCT/US2016/066957

opening 124 is formed as a slot and fluidly communicates with an elongate channel 126 defined by an inner surface 128 of body 102. With reference to Figure 1, it will be appreciated that first opening 124 is disposed on an outer side 130 of body 102. Accordingly, channel 126 opens in a radially outward direction 132 via first opening 124.

5 [0080] Ocular implant 100 may be inserted into Schlemm's canal of a human eye to facilitate the flow of aqueous humor out of the anterior chamber. This flow may include axial flow along Schlemm's canal, flow from the anterior chamber into Schlemm's canal, and flow leaving Schlemm's canal via outlets communicating with Schlemm's canal. When in place within the eye, ocular implant 100 will support trabecular mesh tissue and Schlemm's canal tissue and will provide for improved communication
10 between the anterior chamber and Schlemm's canal (via the trabecular meshwork) and between pockets or compartments along Schlemm's canal. As shown in Figure 1, the implant is preferably oriented so that the first opening 124 is disposed radially outwardly within Schlemm's canal.

[0081] Figure 2A is an enlarged perspective view showing a portion of ocular implant 100 shown in the previous figure. Ocular implant 100 has a body 102 that extends along a generally curved
15 longitudinal axis 134. Body 102 has a plurality of tissue supporting frames 104 and a plurality of spines 106. As shown in Figure 2A, these spines 106 and frames 104 are arranged in a repeating AB pattern in which each A is a tissue supporting frame and each B is a spine. In the embodiment of Figure 2A, one spine extends between each adjacent pair of frames 104.

[0082] The frames 104 of body 102 include a first frame 136 of ocular implant 100 that is disposed
20 between a first spine 140 and a second spine 142. In the embodiment of Figure 2A, first frame 136 is formed as a first strut 144 that extends between first spine 140 and second spine 142. First frame 136 also includes a second strut 146 extending between first spine 140 and second spine 142. In the exemplary embodiment of Figure 2A, each strut undulates in a circumferential direction as it extends longitudinally between first spine 140 and second spine 142.

25 [0083] In the embodiment of Figure 2A, body 102 has a longitudinal radius 150 and a lateral radius 148. Body 102 of ocular implant 100 includes a first edge 120 and a second edge 122 that define a first opening 124. First opening 124 fluidly communicates with an elongate channel 126 defined by an inner surface 128 of body 102. A second opening 138 is defined by a second edge 122A of a first strut 144 and a second edge 122B of a second strut 146. First opening 124, second opening 138 and additional
30 openings defined by ocular implant 100 allow aqueous humor to flow laterally across and/or laterally through ocular implant 100. The outer surfaces 127 of body 102 define a volume 152.

[0084] In some instances, the ocular implant 100 may further include a coating 129 disposed on the inner surfaces 128 and/or outer surfaces 127 of the implant 100, as shown in Figure 2B. While the coating 129 is illustrated on both the outer and inner surfaces 127, 128, the coating 129 may be disposed
35 on only one of the outer surface 127 or the inner surface 128. Further, while the coating 129 is illustrated as extending over the entirety of the outer surface and the inner surface 127, 128, in some embodiments, the coating 129 may cover only a portion of the outer and/or inner surfaces 127, 128. For example, the coating 129 may cover 10% or more, 25% or more, 50% or more, or 75% or more of the surface area of

WO 2017/106517

PCT/US2016/066957

the ocular implant 100. These are just examples. In some instances, the coating 129 may cover less than 10% or more than 75% of the surface area of the implant 100, as desired.

[0085] The coating 129 may be formed of, or otherwise include, a therapeutic agent. In some embodiments, the coating 129 may release the therapeutic agent. The coating 129 may release the therapeutic agent controllably over a period of time. In some embodiments, the therapeutic agent may be applied directly to the ocular implant 100 while in other embodiments, the ocular implant may be dispersed within a matrix material. For example, the therapeutic agent may be dispersed within a biocompatible or biodegradable polymeric material. The concentration of therapeutic agent within the matrix material may vary depending on the desired treatment.

[0086] The biocompatible polymeric material used to form the bioactive agent-polymer composite layer(s) may include any polymeric material capable of forming a solidified composite layer in the presence of the bioactive material. The polymeric material of the present invention may be hydrophilic or hydrophobic, and is, for example, polycarboxylic acids, cellulosic polymers, including cellulose acetate and cellulose nitrate, gelatin, polyvinylpyrrolidone, cross-linked polyvinylpyrrolidone, polyanhydrides including maleic anhydride polymers, polyamides, polyvinyl alcohols, polyolefins, copolymers of vinyl monomers such as EVA, polyvinyl ethers, polyvinyl aromatics, polyethylene oxides, glycosaminoglycans, polysaccharides, polyesters including polyethylene terephthalate, polyacrylamides, polyethers, polyether sulfone, polycarbonate, polyalkylenes including polypropylene, polyethylene and high molecular weight polyethylene, halogenated polyalkylenes including polytetrafluoroethylene, polyurethanes, polyorthoesters, proteins, polypeptides, silicones, siloxane polymers, polylactic acid, polyglycolic acid, polycaprolactone, polyhydroxybutyrate valerate and blends and copolymers thereof as well as other biodegradable, bioabsorbable and biostable polymers and copolymers. Coatings from polymer dispersions such as polyurethane dispersions (BAYHDROL®, etc.) and acrylic latex dispersions are also within the scope of the present invention. The polymer may be a protein polymer, fibrin, collagen and derivatives thereof, polysaccharides such as celluloses, starches, dextrans, alginates and derivatives of these polysaccharides, an extracellular matrix component, hyaluronic acid, or another biologic agent or a suitable mixture of any of these, for example. The coating 129 can include of a single polymer or copolymer. The coating 129 may also include copolymers or physical blends of any of the materials indicated above.

[0087] The therapeutic agents utilized with the ocular implant, may include one or more drugs provided below, either alone or in combination. The drugs utilized may also be the equivalent of, derivatives of, or analogs of one or more of the drugs provided below. The drugs may include but are not limited to pharmaceutical agents including anti-glaucoma medications, ocular agents, antimicrobial agents (e.g., antibiotic, antiviral, antiparasitic, antifungal agents), anti-inflammatory agents (including steroids or non-steroidal anti-inflammatory), biological agents including hormones, enzymes or enzyme-related components, antibodies or antibody-related components, oligonucleotides (including DNA, RNA, short-interfering RNA, antisense oligonucleotides, and the like), DNA/RNA vectors, viruses (either wild type or genetically modified) or viral vectors, peptides, proteins, enzymes, extracellular matrix components,

WO 2017/106517

PCT/US2016/066957

and live cells configured to produce one or more biological components. The use of any particular drug is not limited to its primary effect or regulatory body-approved treatment indication or manner of use.

Drugs also include compounds or other materials that reduce or treat one or more side effects of another drug or therapeutic agent. As many drugs have more than a single mode of action, the listing of any particular drug within any one therapeutic class below is only representative of one possible use of the drug and is not intended to limit the scope of its use with the ophthalmic implant system.

[0088] The therapeutic agents may be combined with any number of excipients as is known in the art. In addition to the biodegradable polymeric excipients discussed above, other excipients may be used, including, but not limited to, benzyl alcohol, ethylcellulose, methylcellulose, hydroxymethylcellulose, cetyl alcohol, croscarmellose sodium, dextrans, dextrose, fructose, gelatin, glycerin, monoglycerides, diglycerides, kaolin, calcium chloride, lactose, lactose monohydrate, maltodextrins, polysorbates, pregelatinized starch, calcium stearate, magnesium stearate, silicon dioxide, cornstarch, talc, and the like. The one or more excipients may be included in total amounts as low as about 1%, 5%, or 10% and in other embodiments may be included in total amounts as high as 50%, 70% or 90%.

[0089] Examples of drugs may include various anti-secretory agents; antimitotics and other anti-proliferative agents, including among others, anti-angiogenesis agents such as angiostatin, anecortave acetate, thrombospondin, VEGF receptor tyrosine kinase inhibitors and anti-vascular endothelial growth factor (anti-VEGF) drugs such as ranibizumab (LUCENTIS®) and bevacizumab (AVASTIN®), pegaptanib (MACUGEN®), sunitinib and sorafenib and any of a variety of known small-molecule and transcription inhibitors having anti-angiogenesis effect; classes of known ophthalmic drugs, including: glaucoma agents, such as adrenergic antagonists, including for example, beta-blocker agents such as atenolol, propranolol, metipranolol, betaxolol, betaxolol hydrochloride, carteolol, levobetaxolol, levobunolol, levobunolol hydrochloride, timolol, timolol hemihydrate, and timolol maleate; adrenergic agonists or sympathomimetic agents such as epinephrine, dipivefrin, clonidine, apraclonidine, and brimonidine; parasympathomimetics or cholinergic agonists such as pilocarpine, carbachol, phospholine iodine, and physostigmine, salicylate, acetylcholine chloride, eserine, diisopropyl fluorophosphate, demecarium bromide); muscarinics; carbonic anhydrase inhibitor agents, including topical and/or systemic agents, for example acetazolamide, brinzolamide, dorzolamide and methazolamide, ethoxzolamide, diamox, and dichlorphenamide; mydriatic-cycloplegic agents such as atropine, cyclopentolate, succinylcholine, homatropine, phenylephrine, scopolamine and tropicamide; prostaglandins such as prostaglandin F₂ alpha, antiprostaglandins, prostaglandin precursors, or prostaglandin analog agents such as bimatoprost, latanoprost, travoprost, tafluprost and unoprostone; docosanoid compounds such as unoprostone.

[0090] Other examples of drugs may also include anti-inflammatory agents including for example glucocorticoids and corticosteroids such as betamethasone, cortisone, dexamethasone, dexamethasone 21-phosphate, methylprednisolone, prednisolone 21-phosphate, prednisolone acetate, prednisolone, flurumetholone, loteprednol, medrysone, fluocinolone acetonide, triamcinolone acetonide, triamcinolone, triamcinolone acetonide, beclomethasone, budesonide, flunisolide, fluorometholone,

WO 2017/106517

PCT/US2016/066957

fluticasone, hydrocortisone, hydrocortisone acetate, loteprednol, rimexolone and non-steroidal anti-inflammatory agents including, for example, diclofenac, flurbiprofen, ibuprofen, bromfenac, nepafenac, and ketorolac, salicylate, indomethacin, ibuprofen, naxopren, piroxicam and nabumetone; anti-infective or antimicrobial agents such as antibiotics including, for example, tetracycline, chlortetracycline, 5 bacitracin, neomycin, polymyxin, gramicidin, cephalixin, oxytetracycline, chloramphenicol, rifampicin, ciprofloxacin, tobramycin, gentamycin, erythromycin, penicillin, sulfonamides, sulfadiazine, sulfacetamide, sulfamethizole, sulfisoxazole, nitrofurazone, sodium propionate, aminoglycosides such as gentamicin and tobramycin; fluoroquinolones such as ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin; bacitracin, erythromycin, fusidic acid, neomycin, polymyxin B, 10 gramicidin, trimethoprim and sulfacetamide; antifungals such as amphotericin B and miconazole; antivirals such as idoxuridine trifluorothymidine, acyclovir, gancyclovir, interferon; antimitotics; immune-modulating agents such as antiallergenics, including, for example, sodium chromoglycate, antazoline, methapyriline, chlorpheniramine, cetrizine, pyrilamine, prophenpyridamine anti-histamine agents such as azelastine, emedastine and levocabastine; immunological drugs (such as vaccines and 15 immune stimulants); MAST cell stabilizer agents such as cromolyn sodium, ketotifen, lodoxamide, nedocrimil, olopatadine and pemirolastciliary body ablative agents, such as gentimicin and cidofovir; and other ophthalmic agents such as verteporfin, proparacaine, tetracaine, cyclosporine and pilocarpine; inhibitors of cell-surface glycoprotein receptors; decongestants such as phenylephrine, naphazoline, tetrahydrazoline; lipids or hypotensive lipids; dopaminergic agonists and/or antagonists such as 20 quinpirole, fenoldopam, and ibopamine; vasospasm inhibitors; vasodilators; antihypertensive agents; angiotensin converting enzyme (ACE) inhibitors; angiotensin-1 receptor antagonists such as olmesartan; microtubule inhibitors; molecular motor (dynein and/or kinesin) inhibitors; actin cytoskeleton regulatory agents such as cyctchalasin, latrunculin, swinholide A, ethacrynic acid, H-7, and Rho-kinase (ROCK) inhibitors; remodeling inhibitors; modulators of the extracellular matrix such as tert-butylhydro-quinolone 25 and AL-3037A; adenosine receptor agonists and/or antagonists such as dicyanopyridines, N-6-cyclophexyladenosine and (R)-phenylisopropyladenosine; serotonin agonists; hormonal agents such as estrogens, estradiol, progestational hormones, progesterone, insulin, calcitonin, parathyroid hormone, peptide and vasopressin hypothalamus releasing factor; growth factor antagonists or growth factors, including, for example, epidermal growth factor, fibroblast growth factor, platelet derived growth factor, 30 transforming growth factor beta, somatotrapin, fibronectin, connective tissue growth factor, bone morphogenic proteins (BMPs); cytokines such as interleukins, CD44, cochlin, and serum amyloids, such as serum amyloid A.

[0091] Other therapeutic agents may include neuroprotective agents such as lubezole, nimodipine and related compounds, and including blood flow enhancers, sodium channels blockers, glutamate 35 inhibitors such as memantine, neurotrophic factors, nitric oxide synthase inhibitors; free radical scavengers or anti-oxidants; chelating compounds; apoptosis-related protease inhibitors; compounds that reduce new protein synthesis; radiotherapeutic agents; photodynamic therapy agents; gene therapy agents;

WO 2017/106517

PCT/US2016/066957

genetic modulators; and dry eye medications such as cyclosporine A, delmulcents, and sodium hyaluronate.

[0092] Other therapeutic agents that may be used include: other beta-blocker agents such as acebutolol, atenolol, bisoprolol, carvedilol, asmolol, labetalol, nadolol, penbutolol, and pindolol; other corticosteroidal and non-steroidal anti-inflammatory agents such aspirin, betamethasone, cortisone, diflunisal, etodolac, fenoprofen, fludrocortisone, flurbiprofen, hydrocortisone, ibuprofen, indomethacine, ketoprofen, meclofenamate, mefenamic acid, meloxicam, methylprednisolone, nabumetone, naproxen, oxaprozin, prednisolone, piroxicam, salsalate, sulindac and tolmetin; COX-2 inhibitors like celecoxib, rofecoxib and Valdecoxib; other immune-modulating agents such as aldesleukin, adalimumab (HUMIRA®), azathioprine, basiliximab, daclizumab, etanercept (ENBREL®), hydroxychloroquine, infliximab (REMICADE®), leflunomide, methotrexate, mycophenolate mofetil, and sulfasalazine; other anti-histamine agents such as loratadine, desloratadine, cetirizine, diphenhydramine, chlorpheniramine, dexchlorpheniramine, clemastine, cyproheptadine, fexofenadine, hydroxyzine and promethazine; other anti-infective agents such as aminoglycosides such as amikacin and streptomycin; anti-fungal agents such as amphotericin B, caspofungin, clotrimazole, fluconazole, itraconazole, ketoconazole, voriconazole, terbinafine and nystatin; anti-malarial agents such as chloroquine, atovaquone, mefloquine, primaquine, quinidine and quinine; anti-mycobacterium agents such as ethambutol, isoniazid, pyrazinamide, rifampin and rifabutin; anti-parasitic agents such as albendazole, mebendazole, thiobendazole, metronidazole, pyrantel, atovaquone, iodoquinaol, ivermectin, paromycin, praziquantel, and trimatrexate; other anti-viral agents, including anti-CMV or anti-herpetic agents such as acyclovir, cidofovir, famciclovir, gangciclovir, valacyclovir, valganciclovir, vidarabine, trifluridine and foscarnet; protease inhibitors such as ritonavir, saquinavir, lopinavir, indinavir, atazanavir, amprenavir and nelfinavir; nucleotide/nucleoside/non-nucleoside reverse transcriptase inhibitors such as abacavir, ddl, 3TC, d4T, ddC, tenofovir and emtricitabine, delavirdine, efavirenz and nevirapine; other anti-viral agents such as interferons, ribavirin and trifluridien; other anti-bacterial agents, including cabapenems like ertapenem, imipenem and meropenem; cephalosporins such as cefadroxil, cefazolin, cefdinir, cefditoren, cephalixin, cefaclor, cefepime, cefoperazone, cefotaxime, cefotetan, cefoxitin, cefpodoxime, cefprozil, ceftaxidime, ceftibuten, ceftizoxime, ceftriaxone, cefuroxime and loracarbef; other macrolides and ketolides such as azithromycin, clarithromycin, dirithromycin and telithromycin; penicillins (with and without clavulanate) including amoxicillin, ampicillin, pivampicillin, dicloxacillin, nafcillin, oxacillin, piperacillin, and ticarcillin; tetracyclines such as doxycycline, minocycline and tetracycline; other anti-bacterials such as aztreonam, chloramphenicol, clindamycin, linezolid, nitrofurantoin and vancomycin; alpha blocker agents such as doxazosin, prazosin and terazosin; calcium-channel blockers such as amlodipine, bepridil, diltiazem, felodipine, isradipine, nifedipine, nisoldipine and verapamil; other anti-hypertensive agents such as clonidine, diazoxide, fenoldopam, hydralazine, minoxidil, nitroprusside, phenoxybenzamine, epoprostenol, tolazoline, treprostinil and nitrate-based agents; anti-coagulant agents, including heparins and heparinoids such as heparin, dalteparin, enoxaparin, tinzaparin and fondaparinux; other anti-coagulant agents such as hirudin, aprotinin, argatroban, bivalirudin, desirudin, lepirudin, warfarin and ximelagatran;

WO 2017/106517

PCT/US2016/066957

anti-platelet agents such as abciximab, clopidogrel, dipyridamole, optifibatide, ticlopidine and tirofiban; prostaglandin PDE-5 inhibitors and other prostaglandin agents such as alprostadil, carboprost, sildenafil, tadalafil and vardenafil; thrombin inhibitors; antithrombogenic agents; anti-platelet aggregating agents; thrombolytic agents and/or fibrinolytic agents such as alteplase, anistreplase, reteplase, streptokinase, tenecteplase and urokinase; anti-proliferative agents such as sirolimus, tacrolimus, everolimus, zotarolimus, paclitaxel and mycophenolic acid; hormonal-related agents including levothyroxine, fluoxymestrone, methyltestosterone, nandrolone, oxandrolone, testosterone, estradiol, estrone, estropipate, clomiphene, gonadotropins, hydroxyprogesterone, levonorgestrel, medroxyprogesterone, megestrol, mifepristone, norethindrone, oxytocin, progesterone, raloxifene and tamoxifen; anti-neoplastic agents, including alkylating agents such as carmustine lomustine, melphalan, cisplatin, fluorouracil³, and procarbazine antibiotic-like agents such as bleomycin, daunorubicin, doxorubicin, idarubicin, mitomycin and plicamycin; anti proliferative agents (such as 1,3-cis retinoic acid, 5-fluorouracil, taxol, rapamycin, mitomycin C and cisplatin); antimetabolite agents such as cytarabine, fludarabine, hydroxyurea, mercaptopurine and 5-fluorouracil (5-FU); immune modulating agents such as aldesleukin, imatinib, rituximab and tositumomab; mitotic inhibitors docetaxel, etoposide, vinblastine and vincristine; radioactive agents such as strontium-89; and other anti-neoplastic agents such as irinotecan, topotecan and mitotane.

[0093] Figure 3 is an additional perspective view showing volume 152 defined by the body of the ocular implant shown in the previous figure. With reference to Figure 3, it will be appreciated that volume 152 extends along a generally curved longitudinal axis 134. Volume 152 has a longitudinal radius 150, a lateral radius 148, and a generally circular lateral cross section 153.

[0094] Figure 4 is a perspective view showing a first plane 154 and a second plane 155 that both intersect ocular implant 100. In Figure 4, first plane 154 is delineated with hatch marks. With reference to Figure 4, it will be appreciated that spines 106 of body 102 are generally aligned with one another and that first plane 154 intersects all spines 106 shown in Figure 4. In the embodiment of Figure 4, body 102 of ocular implant 100 is generally symmetric about first plane 154.

[0095] In the embodiment of Figure 4, the flexibility of body 102 is at a maximum when body 102 is bending along first plane 154, and body 102 has less flexibility when bending along a plane other than first plane 154 (e.g., a plane that intersects first plane 154). For example, in the embodiment shown in Figure 4, body 102 has a second flexibility when bending along second plane 155 that is less than the first flexibility that body 102 has when bending along first plane 154.

[0096] Stated another way, in the embodiment of Figure 4, the bending modulus of body 102 is at a minimum when body 102 is bent along first plane 154. Body 102 has a first bending modulus when bent along first plane 154 and a greater bending modulus when bent along a plane other than first plane 154 (e.g., a plane that intersects first plane 154). For example, in the embodiment shown in Figure 4, body 102 has a second bending modulus when bent along second plane 155 that is greater than the first bending modulus that body 102 has when bent along first plane 154.

WO 2017/106517

PCT/US2016/066957

[0097] Figure 5 is an enlarged perspective view showing a portion of ocular implant 100 shown in the previous figure. In the exemplary embodiment of Figure 5, a bending moment M is being applied to body 102 of ocular implant 100. Bending moment M acts about a first axis 156 that is generally orthogonal to first plane 154. A second axis 158 and a third axis 160 are also shown in Figure 5. Second axis 158 is generally perpendicular to first axis 156. Third axis 160 is skewed relative to first axis 156.

[0098] An inner surface 128 of body 102 defines a channel 126. Body 102 of ocular implant 100 includes a first edge 120 and a second edge 123 that define a first opening 124. Channel 126 of ocular implant 100 fluidly communicates with first opening 124. A second opening 138 is defined by a second edge 122A of a first strut 144 and a second edge 122B of a second strut 146. First opening 124, second opening 138 and additional openings defined by ocular implant 100 allow aqueous humor to flow laterally across and/or laterally through ocular implant 100.

[0099] As shown in Figure 5, ocular implant 100 has a first spine 140 and a second spine 142. First strut 144 and a second strut 146 form a first frame 136 of ocular implant 100 that extends between first spine 140 and second spine 142. In the exemplary embodiment of Figure 5, each strut undulates in a circumferential direction as it extends longitudinally between first spine 140 and second spine 142.

[0100] In the embodiment of Figure 5, the flexibility of body 102 is at a maximum when body 102 is bent by a moment acting about first axis 156, and body 102 has less flexibility when bent by a moment acting about an axis other than first axis 156 (e.g., second axis 158 and third axis 160). Stated another way, the bending modulus of body 102 is at a minimum when body 102 is bent by a moment acting about first axis 156, and body 102 has a greater bending modulus when bent by a moment acting about an axis other than first axis 156 (e.g., second axis 158 and third axis 160).

[0101] Figure 6 is a plan view showing ocular implant 100 shown in the previous figure. In the embodiment of Figure 6, no external forces are acting on body 102 of ocular implant 100, and body 102 is free to assume the generally curved resting shape depicted in Figure 6. Body 102 defines a first opening 124 that is disposed on an outer side 130 of body 102. A channel 126 is defined by the inner surface of body 102 and opens in a radially outward direction 132 via first opening 124. A proximal end 101 of the ocular implant 100 may include an interlocking portion configured to mate with and/or engage a complementary interlocking portion of a delivery tool. Section lines A-A and B-B are visible in Figure 6. Section line A-A intersects a first frame 136 of ocular implant 100. Section line B-B intersects a first spine 140 of ocular implant 100.

[0102] Figure 7A is a lateral cross-sectional view of ocular implant 100 taken along section line A-A shown in the previous figure. Section line A-A intersects a first strut 144 and a second strut 146 of first frame 136 at the point where the circumferential undulation of these struts is at its maximum. Body 102 of ocular implant 100 has a longitudinal radius 150 and a lateral radius 148. An inner surface 128 of body 102 defines a channel 126. A first opening 124 fluidly communicates with channel 126.

[0103] In Figure 7A, first opening 124 in body 102 can be seen extending between first edge 120A of first strut 144 and a first edge 120B of second strut 146. With reference to Figure 7A, it will be appreciated that second strut 146 has a shape that is a mirror image of the shape of first strut 144.

WO 2017/106517

PCT/US2016/066957

[0104] Figure 7B is a lateral cross-sectional view of ocular implant 100 taken along section line B-B shown in the previous figure. Section line B-B intersects first spine 140 of ocular implant 100. Body 102 has a longitudinal radius 150 and a lateral radius 148. In the embodiment of Figure 7B, the center 159 of lateral radius 148 and the center 163 of longitudinal radius 150 are disposed on opposite sides of first spine 140. The center 159 of lateral radius 148 is disposed on a first side of first spine 140. The center 163 of longitudinal radius 150 is disposed on a second side of second spine 142.

[0105] Figure 8 is an enlarged cross-sectional view of ocular implant 100 taken along section line B-B of Figure 6. First spine 140 includes a first major side 161, a second major side 162, a first minor side 164, and second minor side 166. With reference to Figure 8, it will be appreciated that first major side 161 comprises a concave surface 168. Second major side 162 is opposite first major side 161. In the embodiment of Figure 8, second major side 162 comprises a convex surface 170.

[0106] The geometry of the spine provides the ocular implant with flexibility characteristics that may aid in advancing the ocular implant into Schlemm's canal. In the embodiment of Figure 8, first spine 140 has a thickness T1 extending between first major side 161 and second major side 162. Also in the embodiment of Figure 8, first spine 140 has a width W1 extending between first minor side 164 and second minor side 166.

[0107] In some useful embodiments, the spine of an ocular implant in accordance with this detailed description has an aspect ratio of width W1 to thickness T1 greater than about 2. In some particularly useful embodiments, the spine of an ocular implant in accordance with this detailed description has an aspect ratio of width W1 to thickness T1 greater than about 4. In one useful embodiment, the ocular implant has a spine with an aspect ratio of width W1 to thickness T1 of about 5.2.

[0108] A first axis 156, a second axis 158 and a third axis 160 are shown in Figure 8. Second axis 158 is generally perpendicular to first axis 156. Third axis 160 is skewed relative to first axis 156.

[0109] In the embodiment of Figure 8, the flexibility of first spine 140 is at a maximum when first spine 140 is bent by a moment acting about first axis 156. First spine 140 has a first flexibility when bent by a moment acting about first axis 156 and less flexibility when bent by a moment acting about an axis other than first axis 156 (e.g., second axis 158 and third axis 160). For example, first spine 140 has a second flexibility when bent by a moment acting about second axis 158 shown in Figure 8. This second flexibility is less than the first flexibility that first spine 140 has when bent by a moment acting about first axis 156.

[0110] In the embodiment of Figure 8, the bending modulus of first spine 140 is at a minimum when first spine 140 is bent by a moment acting about first axis 156. First spine 140 has a first bending modulus when bent by a moment acting about first axis 156 and a greater bending modulus when bent by a moment acting about an axis other than first axis 156 (e.g., second axis 158 and third axis 160). For example, first spine 140 has a second bending modulus when bent by a moment acting about second axis 158 shown in Figure 8. This second bending modulus is greater than the first bending modulus that first spine 140 has when bent by a moment acting about first axis 156.

WO 2017/106517

PCT/US2016/066957

[0111] Figure 9 is an enlarged cross-sectional view of ocular implant 100 taken along section line A-A of Figure 6. Section line A-A intersects first strut 144 and second strut 146 at the point where the circumferential undulation of these struts is at its maximum.

[0112] Each strut shown in Figure 9 includes a first major side 161, a second major side 162, a first minor side 164, and second minor side 166. With reference to Figure 9, it will be appreciated that each first major side 161 comprises a concave surface 168 and each second major side 162 comprises a convex surface 170.

[0113] In the embodiment of Figure 9, each strut has a thickness T2 extending between first major side 161 and second major side 162. Also in the embodiment of Figure 9, each strut has a width W2 extending between first minor side 164 and second minor side 166. In some useful embodiments, an ocular implant in accordance with this detailed description includes struts having a width W1 that is greater than the width W2 of the struts of the ocular implant.

[0114] In some useful embodiments, the struts of an ocular implant in accordance with this detailed description have an aspect ratio of width W2 to thickness T2 greater than about 2. In some particularly useful embodiments, the struts of an ocular implant in accordance with this detailed description have an aspect ratio of width W2 to thickness T2 greater than about 4. One exemplary ocular implant has struts with an aspect ratio of width W2 to thickness T2 of about 4.4.

[0115] Body 102 of ocular implant 100 has a longitudinal radius 150 and a lateral radius 148. In some useful embodiments, an ocular implant in accordance with this detailed description is sufficiently flexible to assume a shape matching the longitudinal curvature of Schlemm's canal when the ocular implant advanced into the eye. Also in some useful embodiments, a length of the ocular implant is selected so that the implant will extend across a pre-selected angular span when the implant is positioned in Schlemm's canal. Examples of pre-selected angular spans that may be suitable in some applications include 60°, 90°, 150° and 180°. The diameter of an ocular implant in accordance with this detailed description may be selected so that the ocular implant is dimensioned to lie within and support Schlemm's canal. In some useful embodiments, the diameter of the ocular implant ranges between about 0.005 inches (0.127 millimeters) and about 0.04 inches (1.016 millimeters). In some particularly useful embodiments, the diameter of the ocular implant ranges between about 0.005 inches (0.127 millimeters) and about 0.02 inches (0.508 millimeters).

[0116] It is to be appreciated that an ocular implant in accordance with the present detailed description may be straight or curved. If the ocular implant is curved, it may have a substantially uniform longitudinal radius throughout its length, or the longitudinal radius of the ocular implant may vary along its length. Figure 6 shows one example of an ocular implant having a substantially uniform radius of curvature. Figure 10A shows one example of an ocular implant having a longitudinal radius of curvature that varies along the length of the ocular implant. An example of a substantially straight ocular implant is shown in Figure 13.

[0117] Figure 10A is an enlarged perspective view showing a portion of ocular implant 100 shown in the Figures 2 and 4. The ocular implant 100 may further include an intraocular pressure sensor 180

WO 2017/106517

PCT/US2016/066957

mounted to the inner surface 128 of the ocular implant 100 adjacent to an outlet of the implant 100, as shown in Detail A. While the pressure sensor 180 is illustrated as mounted to an inner surface 128 of the ocular implant 100 it is contemplated that the pressure sensor 180 may be mounted within one of the openings 124, 138 or on an outer surface of the ocular implant 100, as desired. The pressure sensor 180 may continuously measure the intraocular pressure of a patient, once the ocular implant 100 has been implanted.

[0118] The pressure sensor 180 may be a Micro-Electro-Mechanical System (MEMS) pressure sensor. While the pressure sensor 180 has been described as a MEMS pressure sensor, it is contemplated that other pressure sensors may be used in place of, or in addition to, a MEMS pressure sensor. In some instances, the pressure sensor 180 may have a width in the range of approximately 0.02 millimeters (20 micrometers) to approximately 1.0 millimeters. However, it is contemplated that the pressure sensors 180 are smaller than 20 micrometers, or larger than 1.0 millimeter. In some instances, the pressure sensor 180 may have a width dimension in the nanometer range. Further, while only a single pressure sensor 180 has been illustrated, the ocular implant 100 may include more than one pressure sensor 180, as desired. For example, a first pressure sensor may be placed at a first end of the ocular implant 100 and a second pressure sensor may be placed at a second end of the ocular implant. In some instances, the pressure sensor 180 may be provided in the channel 128 adjacent to the proximal end 101 of the implant 100, as shown in Figure 10C. It is contemplated that the pressure sensor 180 may include a protective cover to prevent the delivery device (not explicitly shown) from damaging the sensor 180 during delivery of the ocular implant 100, although this is not required.

[0119] MEMS pressure sensors are often formed by anisotropically etching a recess into a back side of a silicon substrate die, leaving a thin flexible diaphragm 182. In operation, at least one surface of the diaphragm 182 is exposed to an input pressure (e.g., the ocular pressure). The diaphragm 182 deflects according to the magnitude of the input pressure, which may be detected by one or more electrical components or sense elements 186 (e.g., piezoresistors) positioned on or embedded within the diaphragm 182. The change in resistance of the piezoresistors 186 is reflected as a change in an output voltage signal from a resistive bridge formed at least in part by the piezoresistors. In some cases, the diaphragm may be made thinner with the addition of support bosses, which may help increase the sensitivity of the diaphragm over a flat plate diaphragm. Circuit elements may be connected so that sensor elements 186 to provide some level of signal processing before providing an output signal to bond pads 188 of the pressure sensor 180. The signal processing may filter, amplify, linearize, calibrate and/or otherwise process the raw sensor signal produced by the sensor elements (e.g., piezoresistors 186). While the sense elements 186 have been described as piezoresistors, it is contemplated that the sense elements may be selected to provide a capacitive pressure sensor 180.

[0120] The pressure sensor 180 may include a first substrate 185 and a second substrate 183, as shown in Figure 10B, which is a cross-section of the illustrative pressure sensor 180 taken at line B-B in Figure 10A. In some instances, the first substrate 185 may be a layered silicon-insulator-silicon substrate or wafer formed with silicon on insulator (SOI) technology, although this is not required. It is

WO 2017/106517

PCT/US2016/066957

contemplated that other substrates may be used, as desired. The first substrate 185 may include a first silicon layer. An insulating, or oxide, layer 187 may be disposed on the first silicon layer 185. In some instances, the insulating layer 187 may be formed from silicon dioxide, silicon nitride, sapphire, and/or any other suitable insulating material. While not explicitly shown, the pressure sensor 180 may include a second silicon layer disposed on the insulating layer. In some instances, the second silicon layer may be thinned or removed such that the oxide layer 187 is exposed at the side facing away from the second substrate 183. Alternatively, and in some cases, the second silicon layer and oxide layer 187 are not provided from the start.

[0121] The second substrate 183 may be any semi-conductor wafer (e.g., silicon or germanium) or other substrate as desired. It is contemplated that either or both the first substrate 185 or the second substrate 183 may be doped with an impurity to provide an n-type or p-type extrinsic semiconductor. For example, the first substrate 185 may be an n-type substrate while the second substrate 183 may be a p-type substrate. The reverse configuration is also contemplated, or both substrates may be doped the same polarity. In some instances, the first substrate 185 and/or the second substrate 183 may include an epitaxial layer.

[0122] A portion of the first substrate 185, such as a portion of the first silicon layer, may be removed, leaving a thin, flexible diaphragm 182 over a cavity or recess 181. In some cases, piezoresistors 186 may be located in or on the diaphragm 182 to measure deflection/stress of the diaphragm 182 to form a pressure sensor. During operation, at least one surface of the diaphragm 182 may be exposed to an input pressure. The diaphragm 182 may then deflect according to a magnitude of the pressure on the diaphragm 182. A deflection of the diaphragm 182 then creates changes in resistance in the piezoresistors 186. A change in resistance of the piezoresistors 186 may be reflected as a change in an output voltage signal of a resistive bridge that is formed at least partially by the piezoresistors 186. The output voltage provides a measure of the input pressure exerted on the diaphragm 182.

[0123] It is contemplated that the second substrate 183 may be flexible to allow the substrate 183 to be mounted flush against the inner surface 128 of the ocular implant 100. Alternatively, or additionally, the second substrate 183 may have a curved outer surface (facing away from the diaphragm 182) shaped to generally correspond to the curved inner surface 128 of the ocular implant 100. It is further contemplated that the materials forming the pressure sensor 180 may be selected such that the pressure sensor 180 is biocompatible.

[0124] As noted above, while the pressure sensor 180 has been described as a MEMS pressure sensor, it is contemplated that pressure sensor 180 may take other suitable forms. In one alternative example, the pressure sensor may be formed in such a way that radio waves can be used to detect changes in pressure without sensor elements incorporated into the device. Such a pressure sensor may include a flexible base substrate, a bottom inductive coil positioned on the base substrate, a layer of pressure sensitive rubber pyramids positioned over the bottom inductive coil, a top inductive coil positioned on top of the rubber pyramids, and a top substrate positioned over the top inductive coil. As a pressure is exerted on the sensor, the inductive coils move close together. Radio waves (from an applied source) reflected by

WO 2017/106517

PCT/US2016/066957

the inductive coils have a lower resonance frequency when the coils are positioned closer together. Thus, the frequency of the radio waves can indicate the distance between the coils which is then correlated to the pressure exerted on the device.

[0125] The pressure sensor 180 may be further provided with an antenna or inductor 184 to allow the data from the pressure sensor 180 to be wirelessly communicated to a readout device. In some instances, the pressure sensor 180 may use radiofrequency communication protocols, such as, but not limited to cellular communication, ZigBee®, Bluetooth®, WiFi®, IrDA, dedicated short range communication (DSRC), EnOcean®, or any other suitable wireless protocols, as desired to transmit the data from the pressure sensor 180 to another device located outside the body. The data may be transmitted to any number so suitably enabled devices, including, but not limited to, cellular phones, tablet or laptop computers, desktop computers, portable handheld devices, such a personal digital assistant (PDA), or a specially designed device, such as, but not limited to a medical device. This may allow a physician, patient, or other interested party to monitor the ocular pressure without the use of a tonometer. In some instances, the pressure data may be automatically transmitted to a physician from the remote device. For example, as shown in Figure 11, once the ocular implant 100 with the pressure sensor 180 has been implanted, an enabled remote device 192 may be brought within communication range of the patient's 190 eye. This may allow the enabled device 192 to receive the ocular pressure data recorded at the pressure sensor 180. The enabled device 192 may be configured to automatically transmit the data to a physician, for example, to a second remote device.

[0126] Figure 12 is a plan view showing an ocular implant 200 having a radius of curvature that varies along its length. A proximal end 201 of the ocular implant 200 may include an interlocking portion configured to mate with and/or engage a complementary interlocking portion of a delivery tool. In the embodiment of Figure 12, ocular implant 200 has an at rest shape that is generally curved. This at rest shape can be established, for example, using a heat-setting process. The ocular implant shape shown in Figure 12 includes a distal radius RA, a proximal radius RC, and an intermediate radius RB. In the embodiment of Figure 12, distal radius RA is larger than both intermediate radius RB and proximal radius RC. Also in the embodiment of Figure 12, intermediate radius RB is larger than proximal radius RC and smaller than distal radius RA. In one useful embodiment, distal radius RA is about 0.320 inches (8.128 millimeters), intermediate radius RB is about 0.225 inches (5.715 millimeters) and proximal radius RC is about 0.205 inches (5.207 millimeters).

[0127] In the embodiment of Figure 12, a distal portion of the ocular implant follows an arc extending across an angle AA. A proximal portion of the ocular implant follows an arc extending across an angle AC. An intermediate portion of the ocular implant is disposed between the proximal portion and the distal portion. The intermediate portion extends across an angle AB. In one useful embodiment, angle AA is about 55 degrees, angle AB is about 79 degrees and angle AC is about 60 degrees.

[0128] Ocular implant 200 may be used in conjunction with a method of treating the eye of a human patient for a disease and/or disorder (e.g., glaucoma). Some such methods may include the step of inserting a core member into a lumen defined by ocular implant 200. The core member may comprise,

WO 2017/106517

PCT/US2016/066957

for example, a wire or tube. The distal end of the ocular implant may be inserted into Schlemm's canal. The ocular implant and the core member may then be advanced into Schlemm's canal until the ocular implant has reached a desired position. In some embodiments, an inlet portion of the implant may be disposed in the anterior chamber of eye while the remainder of the implant extends through the trabecular mesh into Schlemm's canal. The core member may then be withdrawn from the ocular implant, leaving the implant in place to support tissue forming Schlemm's canal. Further details of ocular implant delivery systems may be found in U.S. Application No. 11/943,289, filed November 20, 2007, now U.S. Patent No. 8,512,404, the disclosure of which is incorporated herein by reference.

[0129] The flexibility and bending modulus features of the ocular implant of this invention help ensure proper orientation of the implant within Schlemm's canal. Figure 1 shows the desired orientation of opening 124 when the implant 100 is disposed in Schlemm's canal. As shown, opening 124 faces radially outward. The implant 100 is therefore designed so that it is maximally flexible when bent along a plane defined by the longitudinal axis of implant 100 as shown in Figure 1, and less flexible when bent in other planes, thereby enabling the curved shape of Schlemm's canal to help place the implant in this orientation automatically if the implant is initially placed in Schlemm's canal in a different orientation.

[0130] Figure 13 is a perspective view showing an ocular implant 300 in accordance with an additional embodiment in accordance with the present detailed description. With reference to Figure 13, it will be appreciated that ocular implant 300 has a resting (i.e., unstressed) shape that is generally straight. Ocular implant 300 extends along a longitudinal axis 334 that is generally straight. In some useful embodiments, ocular implant 300 is sufficiently flexible to assume a curved shape when advanced into Schlemm's canal of an eye.

[0131] Ocular implant 300 comprises a body 302. With reference to Figure 13, it will be appreciated that body 302 comprises a plurality of tissue supporting frames 304 and a plurality of spines 306. As shown in Figure 13, these spines 306 and frames 304 are arranged in an alternating pattern in which one spine extends between each adjacent pair of frames 304. The frames 304 of body 302 include a first frame 336 of ocular implant 300 is disposed between a first spine 340 and a second spine 342. In the embodiment of Figure 13, first frame 336 comprises a first strut 344 that extends between first spine 340 and second spine 342. A second strut 346 of first frame also extends between first spine 340 and second spine 342. Each strut undulates in a circumferential direction as it extends longitudinally between first spine 340 and second spine 342.

[0132] An inner surface 328 of body 302 defines a channel 326. Body 302 of ocular implant 300 includes a first edge 320 and a second edge 322 that define a first opening 324. Channel 326 of ocular implant 300 fluidly communicates with first opening 324. First strut 344 of first frame 336 comprises a first edge 325A. Second strut 346 has a first edge 325B. In Figure 13, first opening 324 in body 302 can be seen extending between first edge 325A of first strut 344 and a first edge 325B of second strut 346.

[0133] A first axis 356, a second axis 358 and a third axis 360 are shown in Figure 13. Second axis 358 is generally perpendicular to first axis 356. Third axis 360 is generally skewed relative to first axis 356. The flexibility of body 302 is at a maximum when body 302 is bent by a moment acting about first

WO 2017/106517

PCT/US2016/066957

axis 356, and body 302 has less flexibility when bent by a moment acting about an axis other than first axis 356 (e.g., second axis 358 and third axis 360). Stated another way, in the embodiment of Figure 13, the bending modulus of body 302 is at a minimum when body 302 is bent by a moment acting about first axis 356, and body 302 has a greater bending modulus when bent by a moment acting about an axis other than first axis 356 (e.g., second axis 358 and third axis 360).

[0134] The ocular implant 300 may further include an intraocular pressure sensor 380 mounted to the inner surface 328 of the ocular implant 300. The pressure sensor 380 may be similar in form and function to pressure sensor 180 described above. While the pressure sensor 380 is illustrated as mounted to an inner surface 328 of the ocular implant 300 it is contemplated that the pressure sensor 380 may be mounted within one of the openings 324 or on an outer surface of the ocular implant 300, as desired. The pressure sensor 380 may continuously measure the intraocular pressure of a patient, once the ocular implant 300 has been implanted.

[0135] The pressure sensor 380 may be a Micro-Electro-Mechanical System (MEMS) pressure sensor. While the pressure sensor 380 has been described as a MEMS pressure sensor, it is contemplated that other pressure sensors may be used in place of, or in addition to, a MEMS pressure sensor. MEMS pressure sensors are often formed by anisotropically etching a recess into a back side of a silicon substrate die, leaving a thin flexible diaphragm. In operation, at least one surface of the diaphragm is exposed to an input pressure (e.g., the ocular pressure). The diaphragm deflects according to the magnitude of the input pressure, which may be detected by one or more electrical components or sense elements (e.g., piezoresistors) positioned on or embedded within the diaphragm. The change in resistance of the piezoresistors is reflected as a change in an output voltage signal from a resistive bridge formed at least in part by the piezoresistors. In some cases, the diaphragm may be made thinner with the addition of support bosses, which may help increase the sensitivity of the diaphragm over a flat plate diaphragm. Circuit elements may be connected so that sensor elements to provide some level of signal processing before providing an output signal to bond pads of the pressure sensor. The signal processing may filter, amplify, linearize, calibrate and/or otherwise process the raw sensor signal produced by the sensor elements (e.g., piezoresistors). While the sense elements have been described as piezoresistors, it is contemplated that the sense elements may be selected to provide a capacitive pressure sensor 380.

[0136] The pressure sensor 380 may be further provided with an antenna or inductor to allow the data from the pressure sensor 380 to be wirelessly communicated to a readout device. In some instances, the pressure sensor 380 may use radiofrequency communication protocols, such as, but not limited to cellular communication, ZigBee®, Bluetooth®, WiFi®, IrDA, dedicated short range communication (DSRC), EnOcean®, or any other suitable wireless protocols, as desired to transmit the data from the pressure sensor 380 to another device located outside the body. The data may be transmitted to any number so suitably enabled devices, including, but not limited to, cellular phones, tablet computers, computers, portable handheld devices, such a personal digital assistant (PDA), or a specially designed device. This may allow a physician, patient, or other interested party to monitor the ocular pressure without the use of a tonometer.

WO 2017/106517

PCT/US2016/066957

[0137] Figure 14 is a stylized representation of a medical procedure in accordance with this detailed description. In the procedure of Figure 14, a physician is treating an eye 400 of a patient P. In the procedure of Figure 14, the physician is holding a hand piece of a delivery system 450 in his or her right hand RH. The physician's left hand (not shown) may be used to hold the handle H of a gonio lens 402.

5 Alternatively, some physicians may prefer holding the delivery system hand piece in the left hand and the gonio lens handle H in the right hand RH.

[0138] During the procedure illustrated in Figure 14, the physician may view the interior of the anterior chamber using gonio lens 402 and a microscope 404. Detail A of Figure 14 is a stylized simulation of the image viewed by the physician. A distal portion of a cannula 452 is visible in Detail A.

10 A shadow-like line indicates the location of Schlemm's canal SC which is lying under various tissues (e.g., the trabecular meshwork) that surround the anterior chamber. A distal opening 454 of cannula 452 is positioned near Schlemm's canal SC of eye 400.

[0139] Methods in accordance with this detailed description may include the step of advancing the distal end of cannula 452 through the cornea of eye 400 so that a distal portion of cannula 452 is disposed in the anterior chamber of the eye. Cannula 452 may then be used to access Schlemm's canal of the eye, for example, by piercing the wall of Schlemm's canal with the distal end of cannula 452. Distal opening 454 of cannula 452 may be placed in fluid communication with a lumen defined by Schlemm's canal. The ocular implant may be advanced out of distal opening 454 and into Schlemm's canal. Insertion of the ocular implant into Schlemm's canal may facilitate the flow of aqueous humor out of the anterior chamber of the eye.

20 [0140] Figure 15 is an enlarged perspective view further illustrating delivery system 450 and eye 400 shown in the previous figure. In Figure 15, cannula 452 of delivery system 450 is shown extending through a cornea 426 of eye 400. A distal portion of cannula 452 is disposed inside the anterior chamber defined by cornea 426 of eye 400. In the embodiment of Figure 15, cannula 452 is configured so that a distal opening 454 of cannula 452 can be placed in fluid communication with Schlemm's canal.

25 [0141] In the embodiment of Figure 15, an ocular implant is disposed in a passageway defined by cannula 452. Delivery system 450 includes a mechanism that is capable of advancing and retracting the ocular implant along the length of cannula 452. The ocular implant may be placed in Schlemm's canal of eye 400 by advancing the ocular implant through the distal opening of cannula 452 while the distal opening is in fluid communication with Schlemm's canal.

30 [0142] Figure 16A is a perspective view showing a delivery system 500 including an ocular implant 550 and a cannula 508 defining a passageway that is dimensioned to slidably receive ocular implant 550. Delivery system 500 may be used to advance ocular implant 550 into a target location in the eye of a patient. Examples of target locations that may be suitable in some applications include areas in and around Schlemm's canal, the trabecular meshwork, the suprachoroidal space, and the anterior chamber of the eye. Figure 16B is an enlarged detail view further illustrating ocular implant 550 and cannula 508 of delivery system 500.

WO 2017/106517

PCT/US2016/066957

[0143] Delivery system 500 of Figure 16A is capable of controlling the advancement and retraction of ocular implant 550 within cannula 508. Ocular implant 550 may be placed in a target location (e.g., Schlemm's canal) by advancing the ocular implant through a distal opening 532 of cannula 508 while the distal opening is in fluid communication with Schlemm's canal. In the embodiment of Figure 16A, ocular implant 550 has been advanced through distal opening 532 of cannula 508 for purposes of illustration.

[0144] Delivery system 500 of Figure 16A includes a housing 502, a sleeve 504, and an end cap 510. A tracking wheel 506 extends through a wall of housing 502 in Figure 16A. Tracking wheel 506 is part of a mechanism that is capable of advancing and retracting a delivery tool 552 of delivery system 500. The delivery tool 552 extends through a distal opening of cannula 508 of Figure 16B. Rotating the tracking wheel will cause delivery tool 552 to move in an axial direction along a passageway defined by cannula 508. The axial direction may be in a distal direction D or a proximal direction P. The delivery tool 552 and the mechanism for moving the delivery tool 552 are described in commonly assigned Application Serial No. 62/024,295, which is herein incorporated by reference.

[0145] In the embodiment of Figure 16A, housing 502 is configured to be gripped with one hand while providing control over the axial advancement and retraction of ocular implant via tracking wheel 506. The housing of delivery system 500 results in an advantageous ergonomic relationship of the fingers relative to the hand. This design provides a configuration that will allow a user, such as a physician, to stabilize the device using part of the hand, while leaving the middle or index finger free move independently from the remainder of the hand. The middle or index finger is free to move independently to rotate the wheel for advancing and/or retract the ocular implant.

[0146] Figure 16B is an enlarged detail view further illustrating ocular implant 550 and a cannula 508 of delivery system 500. Cannula 508 comprises a generally tubular member 598 having proximal portion 540, a distal end 534, and a distal portion 544 extending between distal end 534 and proximal portion 540. In the embodiment of Figure 6, distal portion 544 is curved. In some useful embodiments, distal portion 544 is dimensioned and configured to be received in the anterior chamber of the eye.

[0147] Figure 16B shows delivery tool 552 of delivery system 500 extending through distal opening 532 of cannula 508. Delivery tool 552 includes an interlocking portion 560 that is configured to form a connection with a complementary interlocking portion 562 of ocular implant 550, as explained in more detail below. In the embodiment of Figure 16, rotating the tracking wheel will cause delivery tool 552 and ocular implant 550 to move along a path defined by cannula 508. Cannula 508 is sized and configured so that the distal end of cannula 508 can be advanced through the trabecular meshwork of the eye and into Schlemm's canal. Positioning cannula 508 in this way places distal opening 532 in fluid communication with Schlemm's canal. Ocular implant 550 may be placed in Schlemm's canal by advancing the ocular implant through distal opening 532 of cannula 508 while the distal opening is in fluid communication with Schlemm's canal. The distal portion of the cannula may include a cutting portion configured to cut through the trabecular meshwork and the wall of Schlemm's canal, such as by providing distal end 534 with a sharp edge adapted to cut through such tissue.

WO 2017/106517

PCT/US2016/066957

[0148] Figure 17 is a perspective view of a cannula 508 in accordance with the present detailed description. Cannula 508 of Figure 17 comprises a generally tubular member 598 having a central axis 596. Generally tubular member 598 of Figure 17 comprises a proximal portion 540, a distal end 534, and a distal portion 544 extending between distal end 534 and proximal portion 540. A distal opening surface 542 surrounds a distal opening 532 extending through the distal end 534 and through a side wall of cannula 508. A beveled edge 565 is disposed at the distal end of distal opening surface 542, extending from the distal end 534 to a proximal extent 567 of beveled edge 565. Tubular member 598 defines distal opening 532, a proximal opening 536, and a passageway 538 extending between proximal opening 536 and distal opening 532.

[0149] In the embodiment of Figure 17, proximal portion 540 of cannula 508 is substantially straight, distal portion 544 of cannula 508 is curved, and central axis 596 defines a curvature plane 548. Curvature plane 548 may be referred to as a plane of curvature. Curvature plane 548 divides cannula 508 into a first portion PA and a second portion PB. In the embodiment of Figure 17, second portion PB is substantially a mirror image of first portion PA. In Figure 17, distal portion 544 is shown extending between distal end 534 and proximal portion 540 with no intervening elements. In the embodiment of Figure 17, distal portion 544 is curved along its entire length.

[0150] A method in accordance with this detailed description may include the step of advancing the distal end 534 of cannula 508 through the cornea of a human eye so that distal end 534 is disposed in the anterior chamber of the eye. Cannula 508 may then be used to access Schlemm's canal of the eye, for example, by piercing the wall of Schlemm's canal with the distal end 534 of cannula 508. The beveled edge 565 may be inserted into Schlemm's canal to place at least part of distal opening 532 of cannula 508 in communication with Schlemm's canal, as discussed in more detail below. The ocular implant may be advanced out of a distal port of the cannula and into Schlemm's canal.

[0151] In the embodiment of Figure 17, distal portion 544 of cannula 508 defines a trough 554. In some useful embodiments, trough 554 is configured to receive the entire external cross section of an ocular implant as the ocular implant is being advanced into Schlemm's canal. When this is the case, trough 554 may have a depth dimension that is deeper than a width of the ocular implant. This cannula configuration advantageously prevents the ocular implant from intersecting the layers of the trabecular meshwork as the ocular implant is advanced into Schlemm's canal. Trough 554 may also be configured to allow the proximal portion of the ocular implant to be released from the delivery tool, as discussed below.

[0152] The cannula 508 may further include a pressure sensor 580 disposed within the trough 554. The pressure sensor 580 may be similar in form and function to pressure sensor 180 described above. While the pressure sensor 580 is illustrated as mounted within the trough 554 of the cannula, it is contemplated that the pressure sensor 580 may be mounted at other locations within or on the cannula 508. The pressure sensor 580 may provide an instantaneous pressure reading during implantation of the ocular implant 550 or shortly thereafter. In some instances, the pressure reading obtained from the

WO 2017/106517

PCT/US2016/066957

pressure sensor 580 on the cannula 508 can be compared to a pressure reading obtained from a pressure sensor mounted on the ocular implant 550, if so provided.

[0153] The pressure sensor 580 may be a Micro-Electro-Mechanical System (MEMS) pressure sensor. While the pressure sensor 580 has been described as a MEMS pressure sensor, it is contemplated that other pressure sensors may be used in place of, or in addition to, a MEMS pressure sensor. Further, while only a single pressure sensor 580 has been illustrated, the cannula 508 may include more than one pressure sensor 580, as desired. MEMS pressure sensors are often formed by anisotropically etching a recess into a back side of a silicon substrate die, leaving a thin flexible diaphragm. In operation, at least one surface of the diaphragm is exposed to an input pressure (e.g., the ocular pressure). The diaphragm deflects according to the magnitude of the input pressure, which may be detected by one or more electrical components or sense elements (e.g., piezoresistors) positioned on or embedded within the diaphragm. The change in resistance of the piezoresistors is reflected as a change in an output voltage signal from a resistive bridge formed at least in part by the piezoresistors. In some cases, the diaphragm may be made thinner with the addition of support bosses, which may help increase the sensitivity of the diaphragm over a flat plate diaphragm. Circuit elements may be connected so that sensor elements to provide some level of signal processing before providing an output signal to bond pads of the pressure sensor. The signal processing may filter, amplify, linearize, calibrate and/or otherwise process the raw sensor signal produced by the sensor elements (e.g., piezoresistors). While the sense elements have been described as piezoresistors, it is contemplated that the sense elements may be selected to provide a capacitive pressure sensor 580.

[0154] The pressure sensor 580 may be further provided with an antenna or inductor to allow the data from the pressure sensor 580 to be wirelessly communicated to a readout device. In some instances, the pressure sensor 580 may use radiofrequency communication protocols, such as, but not limited to cellular communication, ZigBee®, Bluetooth®, WiFi®, IrDA, dedicated short range communication (DSRC), EnOcean®, or any other suitable wireless protocols, as desired to transmit the data from the pressure sensor 580 to another device located outside the body. The data may be transmitted to any number so suitably enabled devices, including, but not limited to, cellular phones, tablet computers, computers, portable handheld devices, such a personal digital assistant (PDA), or a specially designed device. This may allow a physician, patient, or other interested party to monitor the ocular pressure without the use of a tonometer.

[0155] Figure 18 is a perspective view of an assembly including cannula 508 shown in the previous figure. For purposes of illustration, cannula 508 is cross-sectionally illustrated in Figure 23. In Figure 18, an ocular implant 550 can be seen resting in a passageway 538 defined by cannula 508. With reference to Figure 18, it will be appreciated that distal portion 544 of cannula 508 is curved so that central axis 596 of cannula 508 defines a curvature plane 548. With reference to Figure 23, it will be appreciated that curvature plane 548 divides cannula 508 into a first portion and a second portion PB. Only second portion PB of cannula 508 is shown in the illustrative embodiment of Figure 18.

WO 2017/106517

PCT/US2016/066957

[0156] Figure 19 is a stylized perspective view including the assembly shown in the previous figure. In the embodiment of Figure 19, a distal portion of cannula 508 is shown extending through the wall of Schlemm's canal SC. The distal tip of cannula 508 may include a sharp portion configured for cutting and/or piercing the trabecular meshwork and the wall of Schlemm's canal so that the passageway defined by the cannula can be placed in fluid communication with the lumen defined by Schlemm's canal. With the passageway of the cannula placed in fluid communication with the lumen of Schlemm's canal, ocular implant 550 can be advanced out of the distal opening of the cannula and into Schlemm's canal. In Figure 19, a distal portion of ocular implant 550 can be seen through distal opening 532 of cannula 508.

[0157] For purposes of illustration, a hypothetical window W is cut through the wall of cannula 508 in Figure 19. An interlocking portion 560 of a delivery tool 552 and a complementary interlocking portion 562 of ocular implant 550 are visible through window W. In the embodiment of Figure 19, interlocking portion 560 of delivery tool 552 and complementary interlocking portion 562 of ocular implant 550 are engaging each other so that a proximal end 549 of ocular implant 550 is proximal to the distal end 551 of delivery tool 552. Surface 561 of delivery tool 552 rests against the wall of cannula 508 to prevent interlocking portion 560 of delivery tool 552 and complementary interlocking portion 562 of ocular implant 550 from disengaging one another. When they are connected in this fashion, delivery tool 552 and ocular implant 550 move together as the delivery tool is advanced and retracted relative to cannula 508 by the delivery system mechanism.

[0158] Figure 20 is an enlarged perspective view showing a portion of cannula 508 shown in the previous figure. In some useful embodiments, cannula 508 is curved to achieve substantially tangential entry into Schlemm's canal SC. In the embodiment of Figure 20, cannula 508 is contacting an outer major wall of Schlemm's canal SC at a point of tangency PT. Also in the embodiment of Figure 20, a curved distal portion of cannula 508 is dimensioned to be disposed within the anterior chamber of the eye.

[0159] As shown in Figure 20, the distal tip 534 and beveled edge of the cannula 508 have been inserted into Schlemm's canal up to the proximal extent 567 of beveled edge 565. In this position, ocular implant 550 can be seen extending into trough 554. In some useful embodiments, the ocular implant has a radius of curvature that is larger than the radius of curvature of the cannula. This arrangement ensures that the ocular implant will track along trough 554 as the ocular implant is urged in a distal direction by delivery system 500.

[0160] Figure 21 is an additional perspective view showing ocular implant 550 and cannula 508 shown in the previous figure. By comparing Figure 21 with the previous figure, it will be appreciated that ocular implant 550 has been advanced in a distal direction D while cannula 508 has remained stationary so that a distal portion of ocular implant 550 is disposed inside Schlemm's canal SC. Trough 554 opens into an elongate opening 532 defined by edge 542 at the distal portion of cannula 508. In the embodiment of Figure 21, the elongate opening defined by the cannula provides direct visualization of the ocular implant as it is advanced into Schlemm's canal. A configuration allowing direct visualization of the ocular implant has a number of clinical advantages. During a medical procedure, it is often difficult to monitor the progress of the implant by viewing the implant through the trabecular meshwork. For

WO 2017/106517

PCT/US2016/066957

example, blood reflux may push blood into Schlemm's canal obstructing a physician's view the portion of the implant that has entered Schlemm's canal. With reference to Figure 21, ocular implant 550 tracks along trough 554 as it is advanced distally along cannula 508. The trough opening allows the physician to monitor the progress of the implant by viewing the implant structures as they advance through the trough prior to entering Schlemm's canal. The trough opening also allows the physician to identify the position of the proximal end of the ocular implant with respect to the incision made by the cannula to access Schlemm's canal.

[0161] Figure 22 is an additional stylized perspective view showing ocular implant 550 and cannula 508. In the embodiment of Figure 22, the interlocking portions 560 and 562 of the delivery tool 552 and ocular implant 550, respectively, can be seen entering the distal opening 532 defined by cannula 508. As shown, ocular implant 550 has been advanced in a distal direction D (relative to the embodiment shown in the previous figure) so that more of ocular implant 550 is disposed inside Schlemm's canal SC. Surface 561 opposite interlocking portion 560 of delivery tool 552 still rests against the inner wall of cannula 508 to keep the delivery tool interlocked with ocular implant 550.

[0162] Figure 23 is an additional stylized perspective view showing ocular implant 550 and cannula 508. As shown in Figure 23, the ocular implant 550 and delivery tool 552 have advanced further distally so that delivery tool surface 561 and part of the reduced diameter portion 563 have now passed into opening 532, thereby permitting the delivery tool curved portion 553 to move toward its curved at-rest shape so that the delivery tool engagement surface 560 disengages and moves away from its complementary engagement surface 562 on the ocular implant 550.

[0163] In some useful embodiments, the delivery tool may be colored to provide visual differentiation from the implant. After the disengaging from the ocular implant, cannula 508 and delivery tool 552 can be withdrawn from Schlemm's canal SC leaving the ocular implant 550 in the fully deployed position shown in Figure 23. After delivery of ocular implant 550 is complete, the delivery tool and the cannula may be removed from the eye, leaving at least a distal portion of the ocular implant in Schlemm's canal.

[0164] Figure 24 is a perspective view of Schlemm's canal SC after the cannula (seen in the previous figure) has been withdrawn leaving an inlet portion of ocular implant 550 in the anterior chamber of the eye and the remainder of ocular implant 550 in Schlemm's canal. The presence of ocular implant 550 in Schlemm's canal may facilitate the flow of aqueous humor out of the anterior chamber. This flow may include axial flow along Schlemm's canal, flow from the anterior chamber into Schlemm's canal, and flow leaving Schlemm's canal via outlets communicating with Schlemm's canal. When in place within the eye, ocular implant 550 will support the trabecular meshwork and Schlemm's canal tissue and will provide for improved communication between the anterior chamber and Schlemm's canal (via the trabecular meshwork) and between pockets or compartments along Schlemm's canal.

[0165] In some instances, it may be desirable to deliver an ocular implant to Schlemm's canal in conjunction with another corrective surgery, such as, but not limited to, cataract surgery. When the ocular implant is placed during another surgical procedure, it may be desirable to insert the ocular implant

WO 2017/106517

PCT/US2016/066957

through the same incision used for the other procedure. Figure 25A is a perspective view showing another illustrative delivery system 600 that may be used to advance ocular implant 650 into a target location in the eye of a patient through an incision location created for another procedure, such as, but not limited to cataract surgery. The delivery system 600 may include an ocular implant 650 and a cannula 608 defining a passageway that is dimensioned to slidably receive ocular implant 650. It is contemplated that aspects of delivery system 600 may be similar in form and function to delivery system 500. Examples of target locations that may be suitable in some applications include areas in and around Schlemm's canal, the trabecular meshwork, the suprachoroidal space, and the anterior chamber of the eye. Figure 25B is an enlarged detail view further illustrating ocular implant 650 and cannula 608 of delivery system 600.

[0166] Delivery system 600 of Figure 25A is capable of controlling the advancement and retraction of ocular implant 650 within cannula 608. Ocular implant 650 may be placed in a target location (e.g., Schlemm's canal) by advancing the ocular implant 650 through a distal opening 632 of cannula 608 while the distal opening is in fluid communication with Schlemm's canal. In the embodiment of Figure 25A, ocular implant 650 has been advanced through distal opening 632 of cannula 608 for purposes of illustration.

[0167] Delivery system 600 of Figure 25A includes a housing 602, a sleeve 604, and an end cap 610. A tracking wheel 606 extends through a wall of housing 602 in Figure 25A. Tracking wheel 606 is part of a mechanism that is capable of advancing and retracting a delivery tool 652 of delivery system 600. The delivery tool 652 is slidably disposed within cannula 608 and configured to extend through a distal opening of cannula 608. Rotating the tracking wheel will cause delivery tool 652 to move in an axial direction along a passageway defined by cannula 608. The axial direction may be in a distal direction D or a proximal direction P. Delivery tool 652 may be similar in form and function to delivery tool 152.

[0168] In the embodiment of Figure 25A, housing 602 is configured to be gripped with one hand while providing control over the axial advancement and retraction of ocular implant via tracking wheel 606. The features of housing 602 result in an advantageous ergonomic relationship of the fingers relative to the hand. This design provides a configuration that will allow a user, such as a physician, to stabilize the device using part of the hand, while leaving the middle or index finger free move independently from the remainder of the hand. The middle or index finger is free to move independently to rotate the wheel for advancing and/or retract the ocular implant.

[0169] Figure 25B is an enlarged detail view further illustrating ocular implant 650 and a cannula 608 of delivery system 600. Cannula 608 comprises a generally tubular member 698 having proximal portion 640, an intermediate portion 645, a distal portion 644, and a distal end 634. The intermediate portion 645 may extend distally from a first point 643 distal to the proximal end 641 to a second point 647 proximal to the distal end 634. The distal portion 644 may extend between distally from the second point 647 to distal end 634 of cannula 608 (shown in Figure 28). In the embodiment of Figure 25, both distal portion 644 and intermediate portion 645 may be curved. In some instances, distal portion 644 may have a smaller radius of curvature, and thus a higher curvature, than the intermediate portion 645,

WO 2017/106517

PCT/US2016/066957

although this is not required. In some useful embodiments, distal portion 644 and intermediate portion 645 may be dimensioned and configured to be received in the anterior chamber of the eye.

[0170] In some instances, it may be desirable to place the ocular implant 650 during another ocular procedure, such as, but not limited to cataract surgery. It is contemplated that the optimal position for an incision for cataract surgery may not be the same as the optimal position of an incision for solely placing an ocular implant, such as implant 650, into Schlemm's canal. With previous ocular implant delivery system designs, in order to allow for substantially tangential entry of the cannula into Schlemm's canal two separate incisions may be required when the implant is placed in combination with another ocular procedure. The curved configuration of both the distal portion 644 may be configured to allow for substantially tangential entry of the cannula 608 into Schlemm's canal. It is further contemplated that the curved configuration of the intermediate portion 645 may allow the cannula 608 to be advanced through typical incisions associated with and/or optimized for cataract surgery, such as, but not limited to, a sclerocorneal tunnel incision, while still allowing for substantially tangential entry of the cannula 608 into Schlemm's canal. This may allow for two or more ocular procedures to be performed using a single incision. It is further contemplated that performing multiple procedures through a single incision may reduce patient discomfort and recovery time. Figure 25B shows delivery tool 652 of delivery system 600 extending through distal opening 632 of cannula 608. Delivery tool 652 includes an interlocking portion 660 that is configured to form a connection with a complementary interlocking portion 662 of ocular implant 650, as explained in more detail below. In the embodiment of Figure 25, rotating the tracking wheel will cause delivery tool 652 and ocular implant 650 to move along a path defined by cannula 608. Cannula 608 is sized and configured so that the distal end of cannula 608 can be advanced through the trabecular meshwork of the eye and into Schlemm's canal. Positioning cannula 608 in this way places distal opening 632 in fluid communication with Schlemm's canal. Ocular implant 650 may be placed in Schlemm's canal by advancing the ocular implant through distal opening 632 of cannula 608 while the distal opening is in fluid communication with Schlemm's canal. The distal portion of the cannula 608 may include a cutting portion configured to cut through the trabecular meshwork and the wall of Schlemm's canal, such as by providing distal end 634 with a sharp edge adapted to cut through such tissue.

[0171] Figure 26 is an enlarged perspective view further illustrating delivery system 600 shown in the previous figure and an eye 601. In Figure 26, cannula 608 of delivery system 600 is shown extending through a cornea 603 of eye 601. A distal portion of cannula 608 is disposed inside the anterior chamber defined by cornea 603 of eye 601. In the embodiment of Figure 26, cannula 608 is configured so that a distal opening 632 of cannula 608 can be placed in fluid communication with Schlemm's canal. For example, distal portion 644 and intermediate portion 645 of cannula 608 may be dimensioned and configured such that cannula 608 may be advanced through an incision 607 created for another optical surgical procedure.

[0172] In the embodiment of Figure 26, an ocular implant is disposed in a passageway defined by cannula 608. Delivery system 600 includes a mechanism that is capable of advancing and retracting the

WO 2017/106517

PCT/US2016/066957

ocular implant along the length of cannula 608. The ocular implant may be placed in Schlemm's canal of eye 601 by advancing the ocular implant through the distal opening of cannula 608 while the distal opening is in fluid communication with Schlemm's canal.

[0173] Figure 27 is a perspective view further illustrating delivery system 600 shown in the previous figure. In Figure 27, a portion of housing 602 has been removed for purposes of illustration. Delivery system 600 includes a delivery tool subassembly 670 and a cannula subassembly 680. Delivery tool subassembly 670 includes rotating rack gear 620 and a delivery tool (not shown). In the embodiment of Figure 27, the delivery tool extends into a passageway defined by a cannula 608. Cannula 608 can be seen extending beyond sleeve 604 in Figure 27. Cannula subassembly 680 includes cannula 608, a hub 672, and an extension tube (not shown). In the embodiment of Figure 27, the extension tube of cannula subassembly 680 is disposed inside a lumen defined by rotating rack gear 620.

[0174] Delivery system 600 includes a mechanism 617 that controls the movement of delivery tool subassembly 670. Mechanism 617 includes a number of components that are located inside housing 602, including tracking wheel 606, an idler gear 622, and the rotating rack gear 620. In the embodiment of Figure 27, tracking wheel 606 and idler gear 622 are both rotatably supported by housing 602. Gear teeth on tracking wheel 606 engage gear teeth on idler gear 622, which in turn engage gear teeth on the rotating rack gear 620. Rotating tracking wheel 606 in a counter clockwise direction CCW causes idler gear 622 to rotate in a clockwise direction CW, which in turn causes the rotating rack gear 620 to move in a distal direction D. Rotating tracking wheel 606 in a clockwise direction CW causes idler gear 622 to rotate in a counter clockwise direction CCW, which in turn causes the rotating rack gear 620 to move in a proximal direction P. In other embodiments, the idler gear 622 may be eliminated from the device, which would cause counter-clockwise movement of the tracking wheel to move the rack gear proximally.

[0175] In the embodiment of Figure 27, a sleeve 604 is fixed to cannula subassembly 680. Sleeve 604 may be rotated by the user to change the orientation of cannula 608 with respect to housing 602. The sleeve 604 may include gripping features, such as grooves (as shown), a rubber coating, or other frictional surfaces to facilitate this use. In some applications, correct alignment between the cannula and iris is advantageous to ensure that the core tube and/or ocular implant is advanced at the correct trajectory relative to Schlemm's canal or other anatomy in the eye into which the ocular implant is to be implanted. The device is configured in a manner that keeps the ocular implant aligned within the device during rotation. Selected groups of components are keyed together to ensure that they rotate as a single body while simultaneously allowing axial movement of the ocular implant. In the embodiment of Figure 27, cannula subassembly 680 and delivery tool subassembly 670 may rotate in unison with sleeve 604 relative to housing 602.

[0176] In the embodiment of Figure 27, rotating rack gear 620 is configured to rotate with sleeve 604 while maintaining the ability to move axially in the distal and proximal directions before, during, and after rotation. As the rotating rack gear 620 moves distally and/or proximally, it causes corresponding movement of the delivery tool relative to cannula 608. This movement is transferred to ocular implant 650 when delivery tool 652 is coupled to ocular implant 650. Delivery tool subassembly 670 and cannula

WO 2017/106517

PCT/US2016/066957

subassembly 680 engage one another in a keyed arrangement, as described in more detail below. This keyed arrangement causes delivery tool subassembly 670 and cannula subassembly 680 to maintain a constant rotational orientation relative to each other while, at the same time, allowing delivery tool subassembly 670 to translate in a distal direction D and a proximal direction P relative to cannula subassembly 680.

[0177] In some embodiments, delivery tool 652 is formed from shape memory material (such as, e.g., nitinol), and at least a portion of delivery tool 652 assumes a curved at-rest shape when no external forces are acting on it. Delivery tool 652 can be urged to assume a straightened shape, for example, by inserting delivery tool 652 through a straight portion of the passageway defined by cannula 608. When the delivery tool 652 is confined, such as within cannula 608, the interlocking portion can engage the complementary interlocking portion to join the delivery tool and ocular implant together, and allow the delivery tool and ocular implant to move together through the cannula 608, as described in more detail below.

[0178] Figures 28, 29, and 30 illustrate more detailed views of cannula 608. Figure 28 is a side view of a cannula 608 in accordance with the present detailed description, Figure 29 is an enlarged detail view of cannula 608, and Figure 30 is an enlarged perspective view further illustrating a portion of distal portion 644 of cannula 608. Cannula 608 comprises a generally tubular member 698 having a central axis 696. Generally, tubular member 698 comprises a proximal end 641, a proximal portion 640, an intermediate portion 645, a distal portion 644, and a distal end 634. Cannula 608 may extend a distance D1 between proximal end 641 and distal end 634. Tubular member 698 may have a length along central axis 696 that is longer than distance D1 between proximal end 641 and distal end 634. For purposes of example, It is contemplated that distance D1 may be in the range of 1.50 to 3.50 inches (3.81 to 8.89 centimeters), 2.0 to 3.0 inches (5.08 to 7.62 centimeters) or around 2.50 inches (6.35 centimeters). It is contemplated cannula 608 may span any distance D1 desired. Proximal portion 640 may extend over a distance D2 from proximal end 641 to a point 643 distal to proximal end 641. Proximal portion 640 may be generally straight such that distance D2 is approximately equal to or equal to a length of proximal portion 640 measured along central axis 696. Distance D2 may be in the range of 1.50 to 2.50 inches (3.81 to 6.35 centimeters), 1.75 to 2.25 inches (4.652 to 5.72 centimeters), or around 2.0 inches (5.08 centimeters). Intermediate portion 645 may extend between first point 643 and a second point 647 located proximal to distal end 634 of cannula 608. Intermediate portion 645 may span a distance D3 extending from point 643 and point 647. Distance D3 may be in the range of 0.15 to 0.50 inches (0.38 to 1.27 centimeters), 0.25 to 0.40 inches (0.64 to 1.02 centimeters), or around 0.33 inches (0.84 centimeters). Intermediate portion 645 may have a length along central axis 696 of tubular member 698 that is longer than distance D3. The difference in the length of intermediate portion 645 and the distance D3 may be determined by the degree of curvature of intermediate portion 645, as will be discussed in more detail below. Distal portion 644 may extend between second point 647 and distal end 634. Distal portion 644 may span a distance D4 extending from point 647 and distal end point 634. Distance D4 may be in the range of 0.05 to 0.30 inches (0.13 to 0.76 centimeters), 0.13 to 0.23 inches (0.33 to 0.58 centimeters), or

WO 2017/106517

PCT/US2016/066957

around 0.17 inches (0.43 centimeters). Distal portion 644 may have a length along central axis 696 of tubular member 698 that is longer than distance D4. The difference in the length of distal portion 644 and the distance D4 may be determined by the degree of curvature of distal portion 644, as will be discussed in more detail below.

5 [0179] A distal opening surface 642 surrounds a distal opening 632 extending through the distal end 634 and through a side wall of cannula 608. A beveled edge 665 is disposed at the distal end of distal opening surface 642, extending from the distal end 634 to a proximal extent 667 of beveled edge 665. Tubular member 698 defines distal opening 632, a proximal opening 636, and a passageway 638 extending between proximal opening 636 and distal opening 632.

10 [0180] Proximal portion 640 of cannula 608 is substantially straight while intermediate portion 645 and distal portion 644 of cannula 608 may be curved. In the embodiment of Figure 28, distal portion 644 is curved along its entire length and intermediate portion 645 is curved along its entire length. Intermediate portion 645 may define a curve having a first radius R1 measured from central axis 696 and defining a first radius of curvature. The length of intermediate portion 645 along central axis 696 may be
15 determined by the measure of the arc (in degrees) and the radius of the curve using Equation 1 below:

$$L_{arc} = \theta \left(\frac{\pi}{180} \right) r \quad \text{Equation 1}$$

where L_{arc} is the length of the arc, θ is the angle measure of the arc (in degrees), and r is the radius of the circle. In some instances, the angle measure of intermediate portion 645 may be in the range of 10° to 25°, although other angles are possible. Distal portion 644 may define a curve having a second radius R2 and defining a second radius of curvature. The length of distal portion 644 along central axis 696 may be
20 determined by the measure of the arc (in degrees) and the radius of the curve using Equation 1 above. In some instances, the angle measure of distal portion 644 may be in the range of 90° to 110°, although other angles are possible. It is contemplated that the first radius R1 may be larger than the second radius R2 such that the distal portion 644 has a higher curvature than the intermediate portion 645. This
25 configuration may advance the ocular implant at the correct trajectory relative to Schlemm's canal or other anatomy in the eye into which the ocular implant is to be implanted. For example, the configuration may allow the cannula 608 to be advanced through an incision generally along a major axis of the visible eye and allowing for substantially tangential entry of cannula 608 into Schlemm's canal. It is contemplated that first radius R1 and second radius R2 may be selected to facilitate delivery of implant
30 650 to other anatomical locations.

[0181] Figure 28A is an additional side view and illustrates a sectioned view of the cannula shown in Figure 25. For purposes of example, cannula 608 comprises a generally tubular member 698 having a central axis 696. Generally tubular member 698 comprises a proximal end 641, a proximal portion 640, an intermediate portion 645, a distal portion 644, and a distal end 634. Additionally, for example, the
35 central axis 696 of proximal portion 640 is tangential to the tangential line at first point 643 of intermediate portion 645. Further, the tangential line at second point 647 of intermediate portion 645 is tangential to the tangential line of the second point 647 of distal portion 644. The tangential line at distal

WO 2017/106517

PCT/US2016/066957

end 634 of distal portion 644 and the central axis 696 of proximal portion may have third radius R3, for example, having an angle approximately in the range of 90° to 165°.

[0182] A method in accordance with this detailed description may include the step of advancing the distal end 634 of cannula 608 through the cornea of a human eye so that distal end 634 is disposed in the anterior chamber of the eye. Cannula 608 may then be used to access Schlemm's canal of the eye, for example, by piercing the wall of Schlemm's canal with the distal end 634 of cannula 608. The beveled edge 665 may be inserted into Schlemm's canal to place at least part of distal opening 632 of cannula 608 in communication with Schlemm's canal. For example, cannula 608 may be advanced until the distal tip 634 and beveled edge 665 of cannula 608 have been inserted into Schlemm's canal up to the proximal extent 667 of beveled edge 665. With the passageway of the cannula 608 placed in fluid communication with the lumen of Schlemm's canal, the ocular implant may be advanced out of a distal port of the cannula 608 and into Schlemm's canal.

[0183] In the embodiment of Figure 29 and further illustrated in Figure 30, distal portion 644 of cannula 608 defines a trough 654. In some embodiments, trough 654 is configured to receive the entire external cross section of an ocular implant as the ocular implant is being advanced into Schlemm's canal. When this is the case, trough 654 may have a depth dimension that is deeper than a width of the ocular implant. This cannula configuration advantageously prevents the ocular implant from intersecting the layers of the trabecular meshwork as the ocular implant is advanced into Schlemm's canal. Trough 654 may also be configured to allow the proximal portion of the ocular implant to be released from the delivery tool in a manner similar to trough 554 described above.

[0184] Referring briefly to Figure 25B, while not explicitly shown, during advancement of ocular implant 650 interlocking portion 660 of delivery tool 652 and complementary interlocking portion 662 of ocular implant 650 may be engaged with each other so that a proximal end of ocular implant 650 is proximal to the distal end of delivery tool 652. Surface 661 of delivery tool 652 rests against the wall of cannula 608 to prevent interlocking portion 660 of delivery tool 652 and complementary interlocking portion 662 of ocular implant 650 from disengaging one another. When they are connected in this fashion, delivery tool 652 and ocular implant 650 move together as the delivery tool is advanced and retracted relative to cannula 608 by the delivery system mechanism. In some embodiments, the ocular implant 650 has a radius of curvature that is larger than the radius of curvature of the distal portion 644 of cannula 608. This arrangement ensures that the ocular implant will track along trough 654 as the ocular implant is urged in a distal direction by delivery system 600.

[0185] Once cannula 608 has been positioned in the desired location, ocular implant 650 may be advanced distally while cannula 608 is held stationary. Elongate opening 632 may provide direct visualization of ocular implant 650 as it is advanced into Schlemm's canal. A configuration allowing direct visualization of the ocular implant has a number of clinical advantages. During a medical procedure, it is often difficult to monitor the progress of the implant by viewing the implant through the trabecular meshwork. For example, blood reflux may push blood into Schlemm's canal obstructing a physician's view the portion of the implant that has entered Schlemm's canal. Ocular implant 650 tracks

WO 2017/106517

PCT/US2016/066957

along trough 654 as it is advanced distally along cannula 608. The trough opening allows the physician to monitor the progress of the implant by viewing the implant structures as they advance through the trough prior to entering Schlemm's canal. The trough opening also allows the physician to identify the position of the proximal end of the ocular implant with respect to the incision made by the cannula to access
5 Schlemm's canal.

[0186] Delivery tool 652 may advance ocular implant 650 distally until delivery tool surface 661 and part of the reduced diameter portion 663 have now passed into opening 632, thereby permitting the delivery tool curved portion to move toward its curved at-rest shape so that the delivery tool engagement surface 660 disengages and moves away from its complementary engagement surface 662 on the ocular
10 implant 650. After the disengaging from the ocular implant, cannula 608 and delivery tool 652 can be withdrawn from Schlemm's canal leaving the ocular implant 650 in the fully deployed position. After delivery of ocular implant 650 is complete, the delivery tool 652 and the cannula 608 may be removed from the eye, leaving at least a distal portion of the ocular implant 650 in Schlemm's canal. An inlet portion of ocular implant 650 may be positioned in the anterior chamber of the eye and the remainder of
15 ocular implant 650 in Schlemm's canal. The presence of ocular implant 650 in Schlemm's canal may facilitate the flow of aqueous humor out of the anterior chamber. This flow may include axial flow along Schlemm's canal, flow from the anterior chamber into Schlemm's canal, and flow leaving Schlemm's canal via outlets communicating with Schlemm's canal. When in place within the eye, ocular implant 650 will support the trabecular meshwork and Schlemm's canal tissue and will provide for improved
20 communication between the anterior chamber and Schlemm's canal (via the trabecular meshwork) and between pockets or compartments along Schlemm's canal.

[0187] The cannula 608 may further include a pressure sensor 690 disposed within the trough 654. The pressure sensor 690 may be similar in form and function to pressure sensor 180 described above. While the pressure sensor 690 is illustrated as mounted within the trough 654 of the cannula, it is
25 contemplated that the pressure sensor 690 may be mounted at other locations within or on the cannula 608. The pressure sensor 690 may provide an instantaneous pressure reading during implantation of the ocular implant 650 or shortly thereafter. In some instances, the pressure reading obtained from the pressure sensor 690 on the cannula 608 can be compared to a pressure reading obtained from a pressure sensor mounted on the ocular implant 650, if so provided.

[0188] The pressure sensor 690 may be a Micro-Electro-Mechanical System (MEMS) pressure sensor. While the pressure sensor 690 has been described as a MEMS pressure sensor, it is contemplated that other pressure sensors may be used in place of, or in addition to, a MEMS pressure sensor. Further, while only a single pressure sensor 690 has been illustrated, the cannula 608 may include more than one pressure sensor 690, as desired. MEMS pressure sensors are often formed by anisotropically etching a
30 recess into a back side of a silicon substrate die, leaving a thin flexible diaphragm. In operation, at least one surface of the diaphragm is exposed to an input pressure (e.g., the ocular pressure). The diaphragm deflects according to the magnitude of the input pressure, which may be detected by one or more electrical components or sense elements (e.g., piezoresistors) positioned on or embedded within the

WO 2017/106517

PCT/US2016/066957

diaphragm. The change in resistance of the piezoresistors is reflected as a change in an output voltage signal from a resistive bridge formed at least in part by the piezoresistors. In some cases, the diaphragm may be made thinner with the addition of support bosses, which may help increase the sensitivity of the diaphragm over a flat plate diaphragm. Circuit elements may be connected so that sensor elements to provide some level of signal processing before providing an output signal to bond pads of the pressure sensor. The signal processing may filter, amplify, linearize, calibrate and/or otherwise process the raw sensor signal produced by the sensor elements (e.g., piezoresistors). While the sense elements have been described as piezoresistors, it is contemplated that the sense elements may be selected to provide a capacitive pressure sensor 690.

10 [0189] The pressure sensor 690 may be further provided with an antenna or inductor to allow the data from the pressure sensor 690 to be wirelessly communicated to a readout device. In some instances, the pressure sensor 690 may use radiofrequency communication protocols, such as, but not limited to cellular communication, ZigBee®, Bluetooth®, WiFi®, IrDA, dedicated short range communication (DSRC), EnOcean®, or any other suitable wireless protocols, as desired to transmit the data from the pressure sensor 690 to another device located outside the body. The data may be transmitted to any number so suitably enabled devices, including, but not limited to, cellular phones, tablet computers, computers, portable handheld devices, such a personal digital assistant (PDA), or a specially designed device. This may allow a physician, patient, or other interested party to monitor the ocular pressure without the use of a tonometer.

20 [0190] An ocular implant, such as any of those described above, may lower the intraocular pressure from its initial, or pretreatment, pressure to a second pressure. The second pressure may be lower than the initial or first pressure. For example, the second pressure may be in the range of 65% to 95% of the initial pressure or in the range of 75% to 85% of the initial pressure. The second intraocular pressure may be within the range of 20 to 30 mm Hg or 23 to 28 mm Hg. These ranges are just examples. The ocular implant may lower the intraocular pressure from the initial pressure to a value above 30 mm Hg or below 20 mm Hg.

[0191] In some instances, the intraocular pressure of a patient may need to be lowered beyond the capabilities of an ocular implant, such as any of those described above. In such instances, it may be desirable to administer a therapeutic drug in combination with deploying an ocular implant, such as implant 100, within a portion of Schlemm's canal. The therapeutic agent may be any agent that may be used to reduce intraocular pressure. Some categories of drug therapy for glaucoma may include but are not limited to: (1) Miotics (e.g., pilocarpine, carbachol, and ace-tylcholinesterase inhibitors), (2) Sympathomimetics (e.g., epinephrine and dipivalylepinephrine), (3) Beta-blockers (e.g., betaxolol, levobunolol and timolol), (4) Carbonic anhydrase inhibitors (e.g., acetazolamide, methazolamide and ethoxzolamide), (5) Prostaglandins (e.g., metabolite derivatives of arachidonic acid), and (6) Rho-kinase (ROCK) inhibitors. The Rho family consists of three small guanosine triphosphate (GTP)-binding proteins (RhoA, RhoB, RhoC), which regulate aspects of cell shape, motility, proliferation, and apoptosis throughout the body. ROCK inhibitors may work by relaxing the trabecular meshwork through inhibition

WO 2017/106517

PCT/US2016/066957

of the actin cytoskeleton contractile tone of smooth muscle. This may result in increased aqueous outflow directly through the trabecular meshwork, achieving lower intraocular pressures in a range similar to prostaglandins. In some instances, ROCK inhibitors may improve blood flow to the optic nerve, increase ganglion cell survival, and reduce bleb scarring in glaucoma surgery. It is contemplated that other therapeutic agents, such as those described with respect to Figure 2B, may also be administered in combination with the delivery of an ocular implant.

[0192] The therapeutic agent may be administered to a patient before or after the implantation of the ocular implant, as desired. When administered after the implantation of an ocular implant, the therapeutic agent may further lower the intraocular pressure from the second pressure (which is lower than the initial pressure) to a third pressure lower than both the initial pressure and the second pressure. For example, the second pressure may be in the range of 65% to 95% of the second pressure (e.g., the lower pressure resulting from the delivery of the ocular implant) or in the range of 75% to 85% of the second pressure. The second intraocular pressure may be within the range of 13 to 23 mm Hg or 15 to 20 mm Hg. These ranges are just examples. The ocular implant may lower the intraocular pressure from the initial pressure to a value above 23 mm Hg or below 15 mm Hg.

[0193] Figure 31 is a schematic illustration of a kit 700 which may include a delivery device 702, ocular implant 704, and a therapeutic agent 706. The ocular implant 706 may be any of the ocular implants described above. The delivery device 704 may be a delivery system such as any of those described above. The delivery device 704 may include a cannula, such as cannulas 452 or 508, and a delivery tool, such as delivery tool 552. Reference to specific embodiments is intended for illustrative purposes only and is not intended to limit the component of kit 700 to any particular embodiment. The therapeutic agent 706 may be a drug intended for the treatment of glaucoma including, but not limited to: (1) Miotics (e.g., pilocarpine, carbachol, and ace-tylcholinesterase inhibitors), (2) Sympathomimetics (e.g., epinephrine and dipivalylepinephrine), (3) Beta-blockers (e.g., betaxolol, levobunolol and timolol), (4) Carbonic anhydrase inhibitors (e.g., acetazolamide, methazolamide and ethoxzolamide), (5) Prostaglandins (e.g., metabolite derivatives of arachidonic acid), and (6) Rho-kinase (ROCK) inhibitors. The therapeutic agent 706 may be provided with a delivery device, such as but not limited to, an eye dropper, syringe, needle, etc. However, if the therapeutic agent is intended for oral delivery, a drug delivery device may not be necessary. While the therapeutic agent 706 is illustrated as a separate component of the kit 700, it is contemplated that the therapeutic agent 706 may be provided as a part of the delivery device 702 and/or implant 704 (e.g., such as a drug eluting coating disposed on a surface of the implant).

[0194] Components of ocular device may be made from a metal, metal alloy, polymer (some examples of which are disclosed below), a metal-polymer composite, ceramics, combinations thereof, and the like, or other suitable material. Some examples of suitable polymers may include polytetrafluoroethylene (PTFE), ethylene tetrafluoroethylene (ETFE), fluorinated ethylene propylene (FEP), polyoxymethylene (POM, for example, DELRIN® available from DuPont), polyether block ester, polyurethane (for example, Polyurethane 85A), polypropylene (PP), polyvinylchloride (PVC), polyether-

WO 2017/106517

PCT/US2016/066957

ester (for example, ARNITEL® available from DSM Engineering Plastics), ether or ester based copolymers (for example, utylene/poly(alkylene ether) phthalate and/or other polyester elastomers such as HYTREL® available from DuPont), polyamide (for example, DURETHAN® available from Bayer or CRISTAMID® available from Elf Atochem), elastomeric polyamides, block polyamide/ethers, polyether block amide (PEBA, for example available under the trade name PEBAX®), ethylene vinyl acetate copolymers (EVA), silicones, polyethylene (PE), Marlex high-density polyethylene, Marlex low-density polyethylene, linear low density polyethylene (for example REXELL®), polyester, polybutylene terephthalate (PBT), polyethylene terephthalate (PET), polytrimethylene terephthalate, polyethylene naphthalate (PEN), polyetheretherketone (PEEK), polyimide (PI), polyetherimide (PEI), polyphenylene sulfide (PPS), polyphenylene oxide (PPO), poly paraphenylene terephthalamide (for example, KEVLAR®), polysulfone, nylon, nylon-12 (such as GRILAMID® available from EMS American Grilon), perfluoro(propyl vinyl ether) (PFA), ethylene vinyl alcohol, polyolefin, polystyrene, epoxy, polyvinylidene chloride (PVdC), poly(styrene-b-isobutylene-b-styrene) (for example, SIBS and/or SIBS 50A), polycarbonates, ionomers, biocompatible polymers, other suitable materials, or mixtures, combinations, copolymers thereof, polymer/metal composites, and the like. In some embodiments the sheath can be blended with a liquid crystal polymer (LCP). For example, the mixture can contain up to about 6 percent LCP.

[0195] Some examples of suitable metals and metal alloys include stainless steel, such as 304V, 304L, and 316LV stainless steel; mild steel; nickel-titanium alloy such as linear-elastic and/or super-elastic nitinol; other nickel alloys such as nickel-chromium-molybdenum alloys (e.g., UNS: N06625 such as INCONEL® 625, UNS: N06022 such as HASTELLOY® C-22®, UNS: N10276 such as HASTELLOY® C276®, other HASTELLOY® alloys, and the like), nickel-copper alloys (e.g., UNS: N04400 such as MONEL® 400, NICKELVAC® 400, NICORROS® 400, and the like), nickel-cobalt-chromium-molybdenum alloys (e.g., UNS: R30035 such as MP35-N® and the like), nickel-molybdenum alloys (e.g., UNS: N10665 such as HASTELLOY® ALLOY B2®), other nickel-chromium alloys, other nickel-molybdenum alloys, other nickel-cobalt alloys, other nickel-iron alloys, other nickel-copper alloys, other nickel-tungsten or tungsten alloys, and the like; cobalt-chromium alloys; cobalt-chromium-molybdenum alloys (e.g., UNS: R30003 such as ELGILOY®, PHYNOX®, and the like); platinum enriched stainless steel; titanium; combinations thereof; and the like; or any other suitable material.

[0196] As alluded to herein, within the family of commercially available nickel-titanium or nitinol alloys, is a category designated "linear elastic" or "non-super-elastic" which, although may be similar in chemistry to conventional shape memory and super elastic varieties, may exhibit distinct and useful mechanical properties. Linear elastic and/or non-super-elastic nitinol may be distinguished from super elastic nitinol in that the linear elastic and/or non-super-elastic nitinol does not display a substantial "superelastic plateau" or "flag region" in its stress/strain curve like super elastic nitinol does. Instead, in the linear elastic and/or non-super-elastic nitinol, as recoverable strain increases, the stress continues to increase in a substantially linear, or a somewhat, but not necessarily entirely linear relationship until plastic deformation begins or at least in a relationship that is more linear than the super elastic plateau

WO 2017/106517

PCT/US2016/066957

and/or flag region that may be seen with super elastic nitinol. Thus, for the purposes of this disclosure linear elastic and/or non-super-elastic nitinol may also be termed “substantially” linear elastic and/or non-super-elastic nitinol.

[0197] In some cases, linear elastic and/or non-super-elastic nitinol may also be distinguishable from super elastic nitinol in that linear elastic and/or non-super-elastic nitinol may accept up to about 2-5% strain while remaining substantially elastic (e.g., before plastically deforming) whereas super elastic nitinol may accept up to about 8% strain before plastically deforming. Both of these materials can be distinguished from other linear elastic materials such as stainless steel (that can also can be distinguished based on its composition), which may accept only about 0.2 to 0.44 percent strain before plastically deforming.

[0198] In some embodiments, the linear elastic and/or non-super-elastic nickel-titanium alloy is an alloy that does not show any martensite/austenite phase changes that are detectable by differential scanning calorimetry (DSC) and dynamic metal thermal analysis (DMTA) analysis over a large temperature range. For example, in some embodiments, there may be no martensite/austenite phase changes detectable by DSC and DMTA analysis in the range of about –60 degrees Celsius (°C) to about 120 °C in the linear elastic and/or non-super-elastic nickel-titanium alloy. The mechanical bending properties of such material may therefore be generally inert to the effect of temperature over this very broad range of temperature. In some embodiments, the mechanical bending properties of the linear elastic and/or non-super-elastic nickel-titanium alloy at ambient or room temperature are substantially the same as the mechanical properties at body temperature, for example, in that they do not display a super-elastic plateau and/or flag region. In other words, across a broad temperature range, the linear elastic and/or non-super-elastic nickel-titanium alloy maintains its linear elastic and/or non-super-elastic characteristics and/or properties.

[0199] In some embodiments, the linear elastic and/or non-super-elastic nickel-titanium alloy may be in the range of about 50 to about 60 weight percent nickel, with the remainder being essentially titanium. In some embodiments, the composition is in the range of about 54 to about 57 weight percent nickel. One example of a suitable nickel-titanium alloy is FHP-NT alloy commercially available from Furukawa Techno Material Co. of Kanagawa, Japan. Some examples of nickel titanium alloys are disclosed in U.S. Patent Nos. 5,238,004 and 6,508,803, which are incorporated herein by reference. Other suitable materials may include ULTANIUM™ (available from Neo-Metrics) and GUM METAL™ (available from Toyota). In some other embodiments, a superelastic alloy, for example a superelastic nitinol can be used to achieve desired properties.

[0200] This application is related to U.S. Patent No. 7,740,604, issued June 22, 2010, and also U.S. Application No. 62/110,293, filed January 30, 2015, the disclosures of which are incorporated by reference as if fully set forth herein.

[0201] It is to be understood that even though numerous characteristics of various embodiments have been set forth in the foregoing description, together with details of the structure and function of various embodiments, this detailed description is illustrative only, and changes may be made in detail, especially

WO 2017/106517

PCT/US2016/066957

in matters of structure and arrangements of parts illustrated by the various embodiments to the full extent indicated by the broad general meaning of the terms in which the appended claims are expressed.

WO 2017/106517

PCT/US2016/066957

CLAIMS

What is claimed is:

1. A method for reducing intraocular pressure in a patient, the method comprising;
5 deploying an ocular implant adapted to reside at least partially in a portion of Schlemm's canal of an eye, the implant comprising:
 a tubular body having an inner surface and an outer surface, the tubular body extending in a curved volume whose longitudinal axis forms an arc of a circle; and
 a plurality of open areas and strut areas formed in the tubular body, the strut areas
10 surrounding the plurality of open areas; and
 the tubular body having a diameter of between 0.005 inches and 0.04 inches;
 wherein the ocular implant is configured to lower the intraocular pressure from an initial to a second pressure within a first range; and
 administering a therapeutic agent comprising a Rho kinase (ROCK) inhibitor to the patient to
15 lower an intraocular pressure to a third pressure within a second range, the third pressure lower than the second pressure.
2. The method of claim 1, wherein deploying the ocular implant comprises:
 inserting a distal end of a cannula through an incision in the eye and into an anterior chamber of
20 the eye;
 placing the distal opening of the cannula into fluid communication with Schlemm's canal such that the cannula enters Schlemm's canal in a substantially tangential orientation;
 advancing the ocular implant distally through the cannula with a delivery tool engaged with the ocular implant, a proximal portion of the ocular implant engaging the delivery tool proximal to a distal
25 portion of the delivery tool; and
 disengaging the ocular implant and the delivery tool when the proximal portion of the ocular implant reaches distal opening of the cannula.
3. The method of claim 1, wherein the first range is approximately 20 to 30 mm Hg.
30
4. The method of claim 3, wherein the first range is approximately 23 to 28 mm Hg.
5. The method of claim 1, wherein the second range is approximately 13 to 23 mm Hg.
- 35 6. The method of claim 5, wherein the second range is approximately 15 to 20 mm Hg.
7. The method of claim 1, wherein the implant further comprises a first pressure sensor disposed on the inner surface of the tubular body.

WO 2017/106517

PCT/US2016/066957

8. A method for reducing intraocular pressure in a patient, the method comprising;
deploying an ocular implant adapted to reside at least partially in a portion of Schlemm's canal of
an eye, the implant comprising:

5 a tubular body having an inner surface and an outer surface, the tubular body extending in
a curved volume whose longitudinal axis forms an arc of a circle; and

a plurality of open areas and strut areas formed in the tubular body, the strut areas
surrounding the plurality of open areas; and

the tubular body having a diameter of between 0.005 inches and 0.04 inches;

10 wherein the ocular implant is configured to lower the intraocular pressure to a second pressure
less than the initial pressure; and

administering a therapeutic agent comprising a Rho kinase (ROCK) inhibitor to the patient to
lower an intraocular pressure from an initial to a third pressure, the third pressure less than the second
pressure.

15

9. The method of claim 8, wherein deploying the ocular implant comprises:
inserting a distal end of a cannula through an incision in the eye and into an anterior chamber of
the eye;

20 placing the distal opening of the cannula into fluid communication with Schlemm's canal such
that the cannula enters Schlemm's canal in a substantially tangential orientation;

advancing the ocular implant distally through the cannula with a delivery tool engaged with the
ocular implant, a proximal portion of the ocular implant engaging the delivery tool proximal to a distal
portion of the delivery tool; and

25 disengaging the ocular implant and the delivery tool when the proximal portion of the ocular
implant reaches distal opening of the cannula.

10. The method of claim 8, wherein the second pressure is approximately 65 to 95% of the initial
pressure.

30 11. The method of claim 10, wherein the second pressure is approximately 75 to 85% of the initial
pressure.

12. The method of claim 8, wherein the third pressure is approximately 65 to 95% of the second
pressure.

35

13. The method of claim 8, wherein the third pressure is approximately 75 to 85% of the second
pressure.

WO 2017/106517

PCT/US2016/066957

14. The method of claim 8, wherein the implant further comprises a first pressure sensor disposed on the inner surface of the tubular body.

15. A kit for reducing intraocular pressure in a patient, the kit comprising:

5 an ocular implant adapted to reside at least partially in a portion of Schlemm's canal of an eye;

a cannula defining a passageway extending from a proximal end to a distal end, the cannula having a distal opening extending through a side wall and the distal end of the cannula to form a trough, a curved distal portion, a curved intermediate portion, and a proximal portion; and

a delivery tool having a distal interlocking portion engaging a complementary interlocking

10 portion of the ocular implant;

a therapeutic agent comprising a Rho kinase (ROCK) inhibitor.

16. The kit of claim 15, further comprising a therapeutic agent delivery device.

15 17. The kit of claim 15, wherein the therapeutic agent delivery device comprises an eye dropper.

18. The kit of claim 15, wherein the ocular implant comprises:

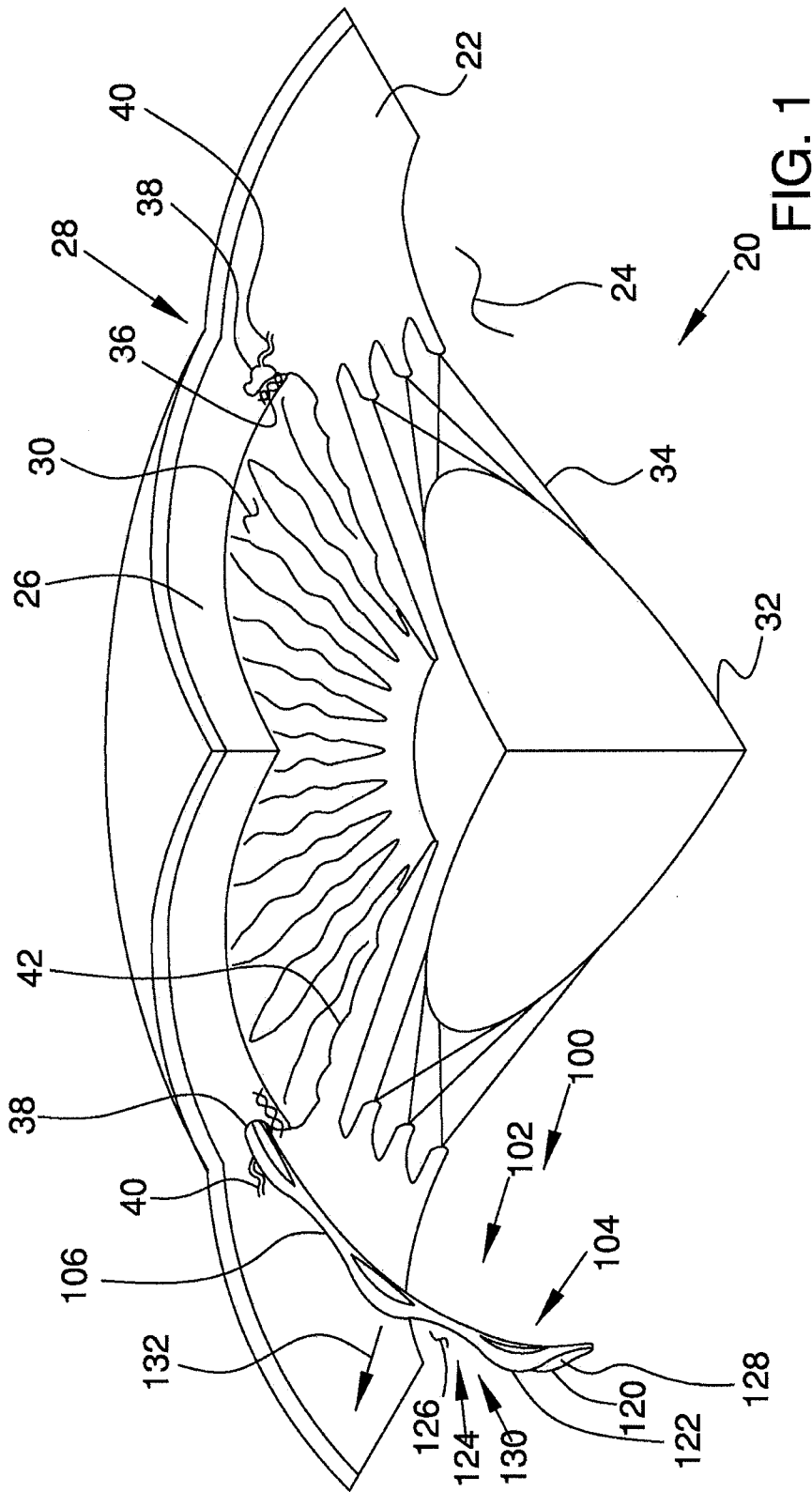
a tubular body having an inner surface and an outer surface, the tubular body extending in a curved volume whose longitudinal axis forms an arc of a circle; and

20 a plurality of open areas and strut areas formed in the tubular body, the strut areas surrounding the plurality of open areas; and

the tubular body having a diameter of between 0.005 inches and 0.04 inches.

19. The kit of claim 18, wherein the ocular implant further comprises a first pressure sensor disposed
25 on the inner surface of the tubular body.

20. The kit of claim 15, wherein the therapeutic agent is disposed on a surface of the ocular implant.



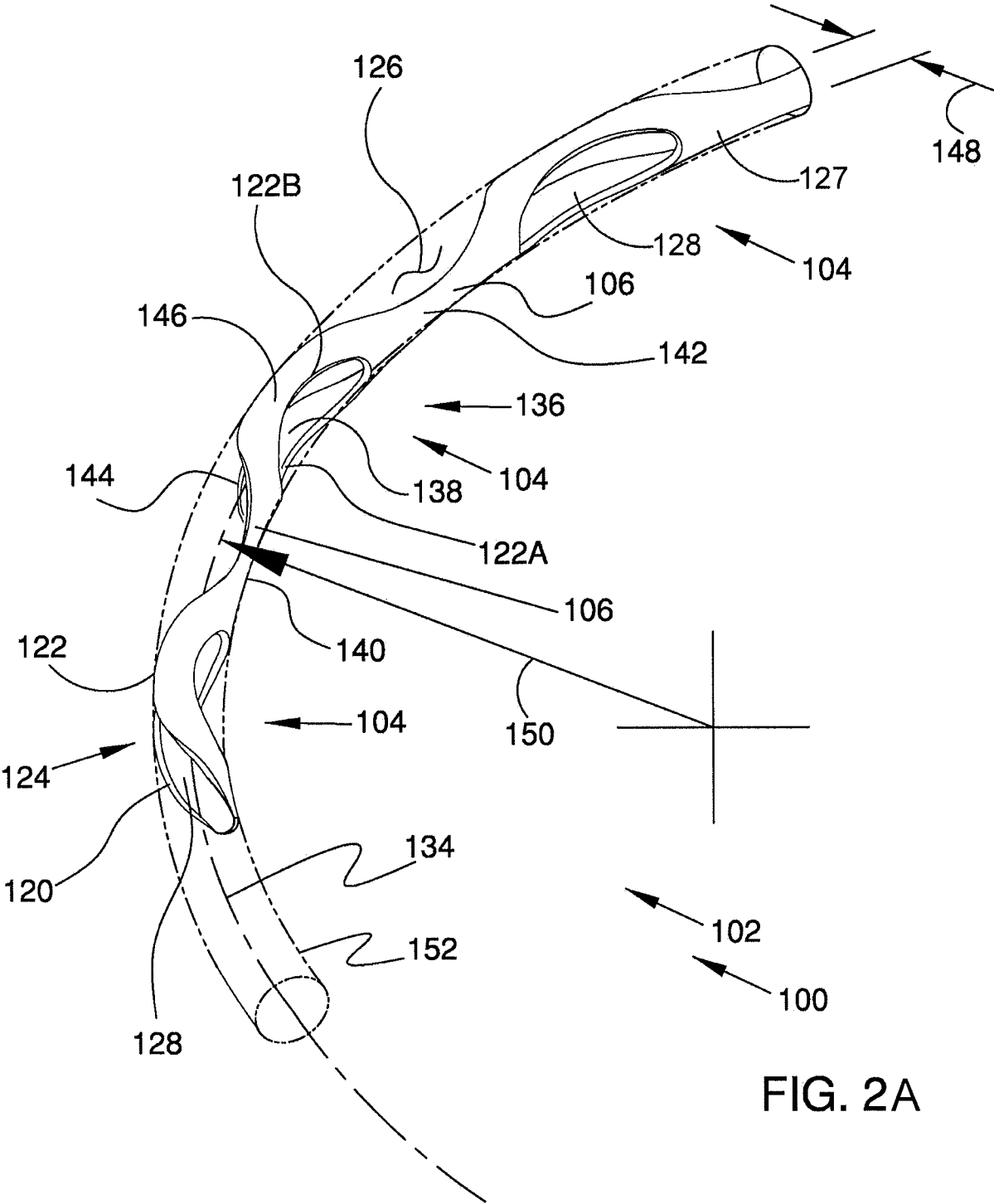
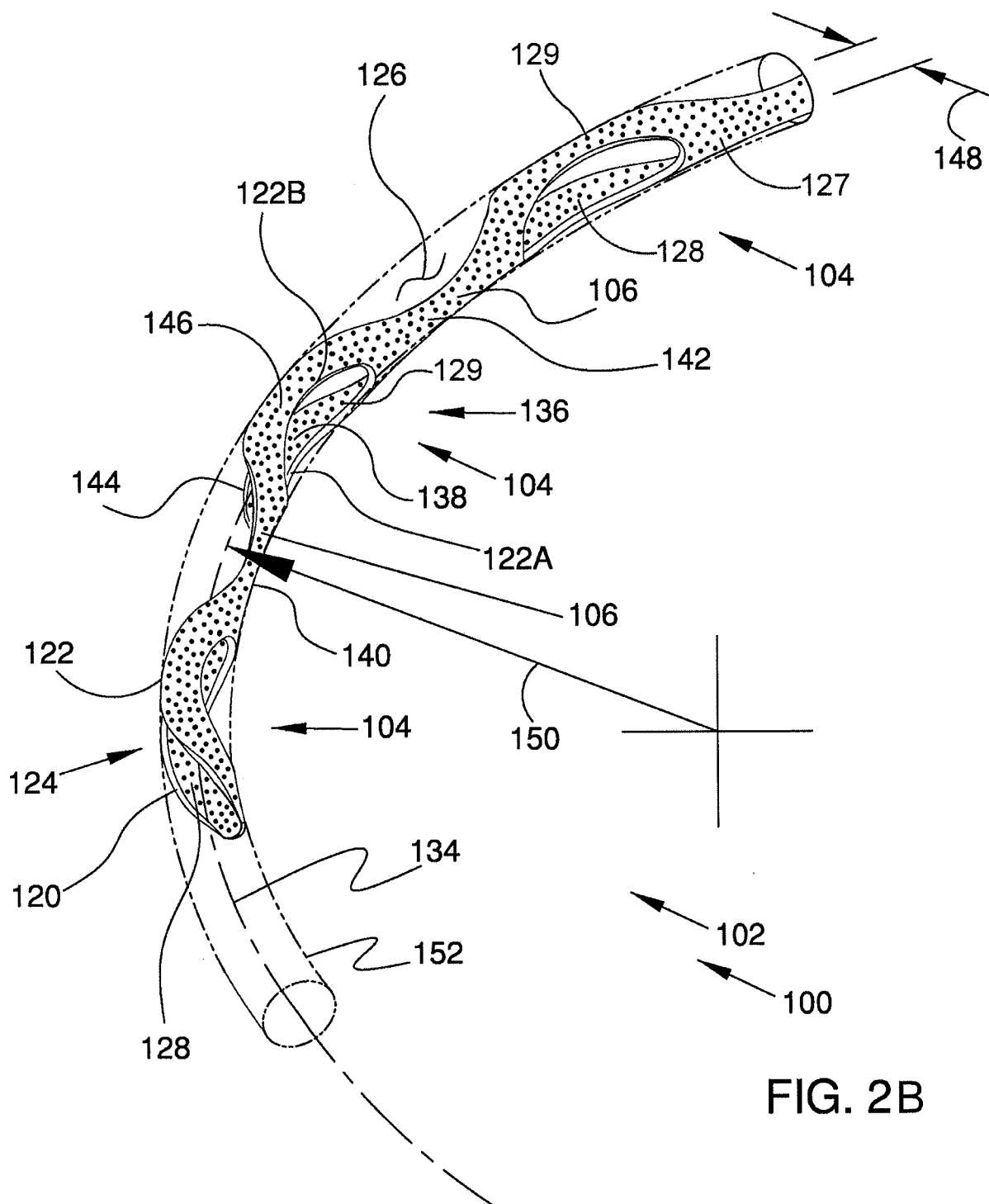


FIG. 2A

3 / 35



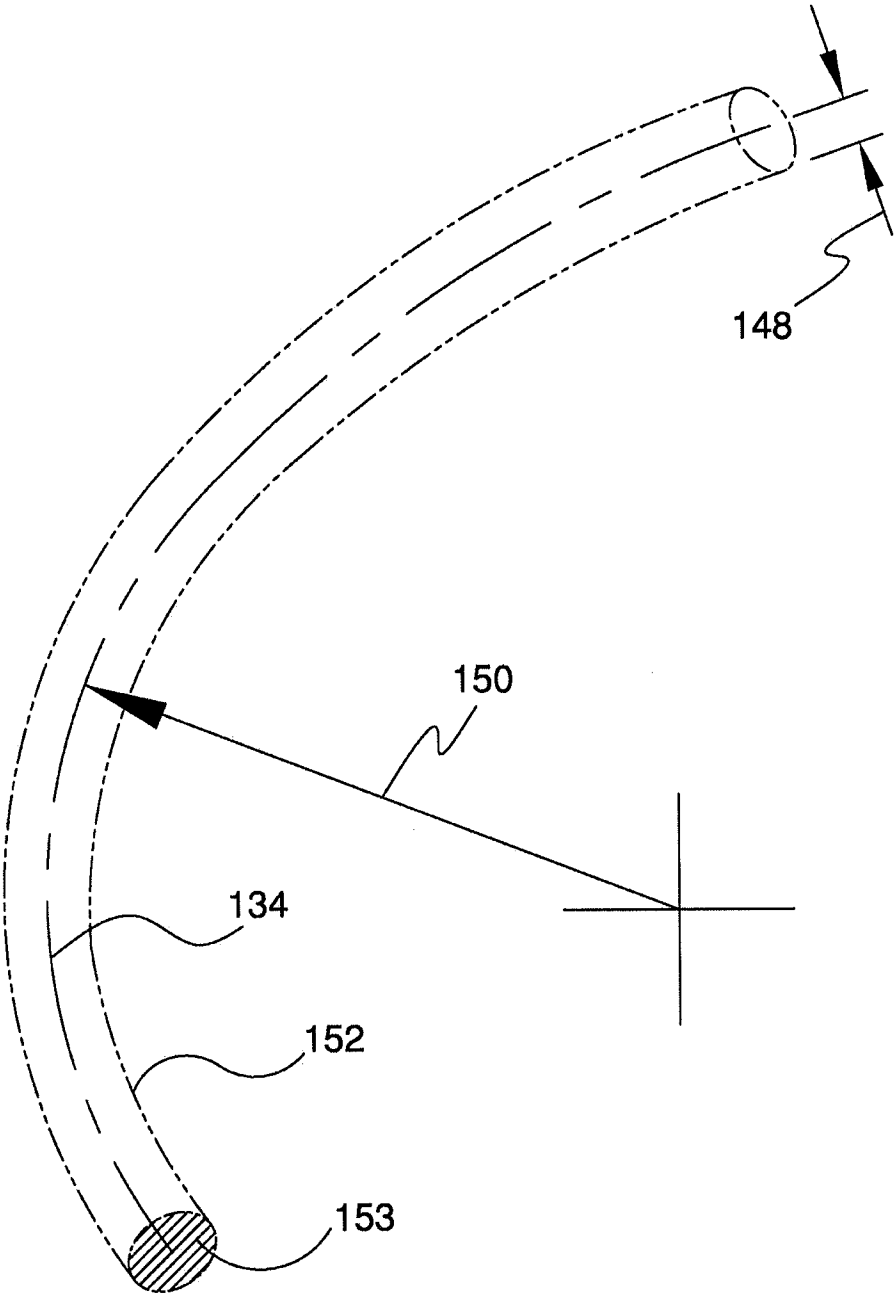


FIG. 3

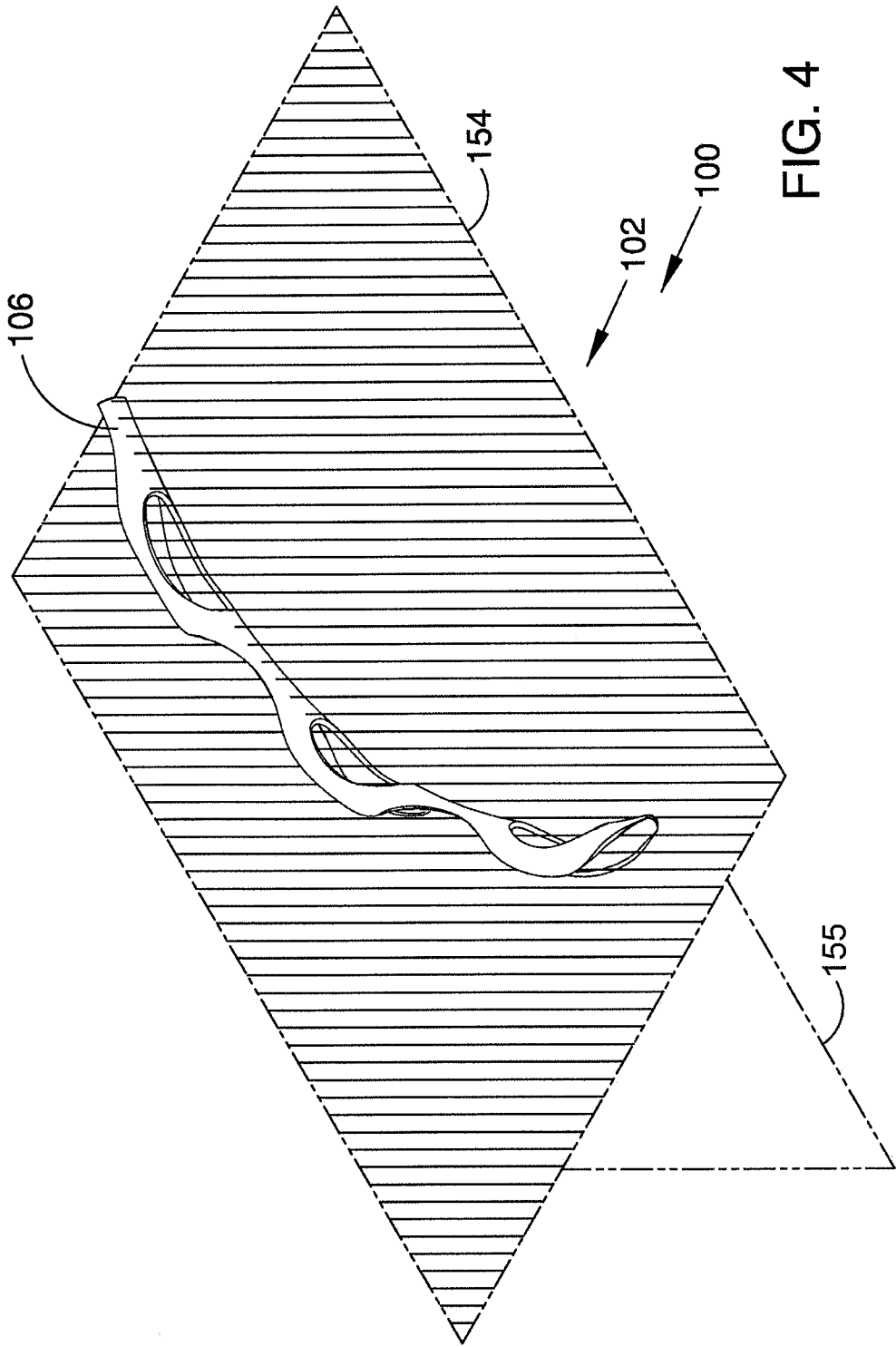


FIG. 4

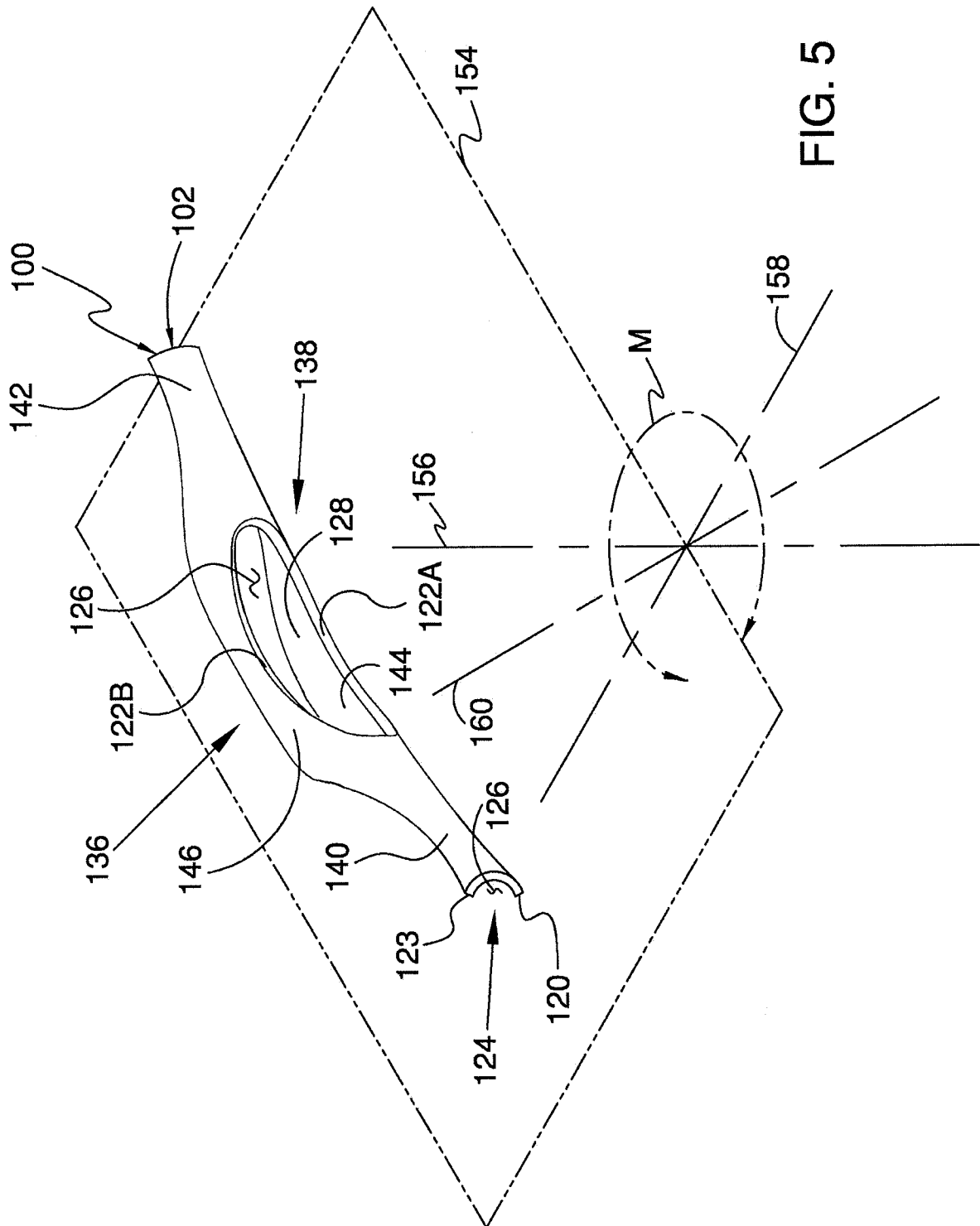


FIG. 5

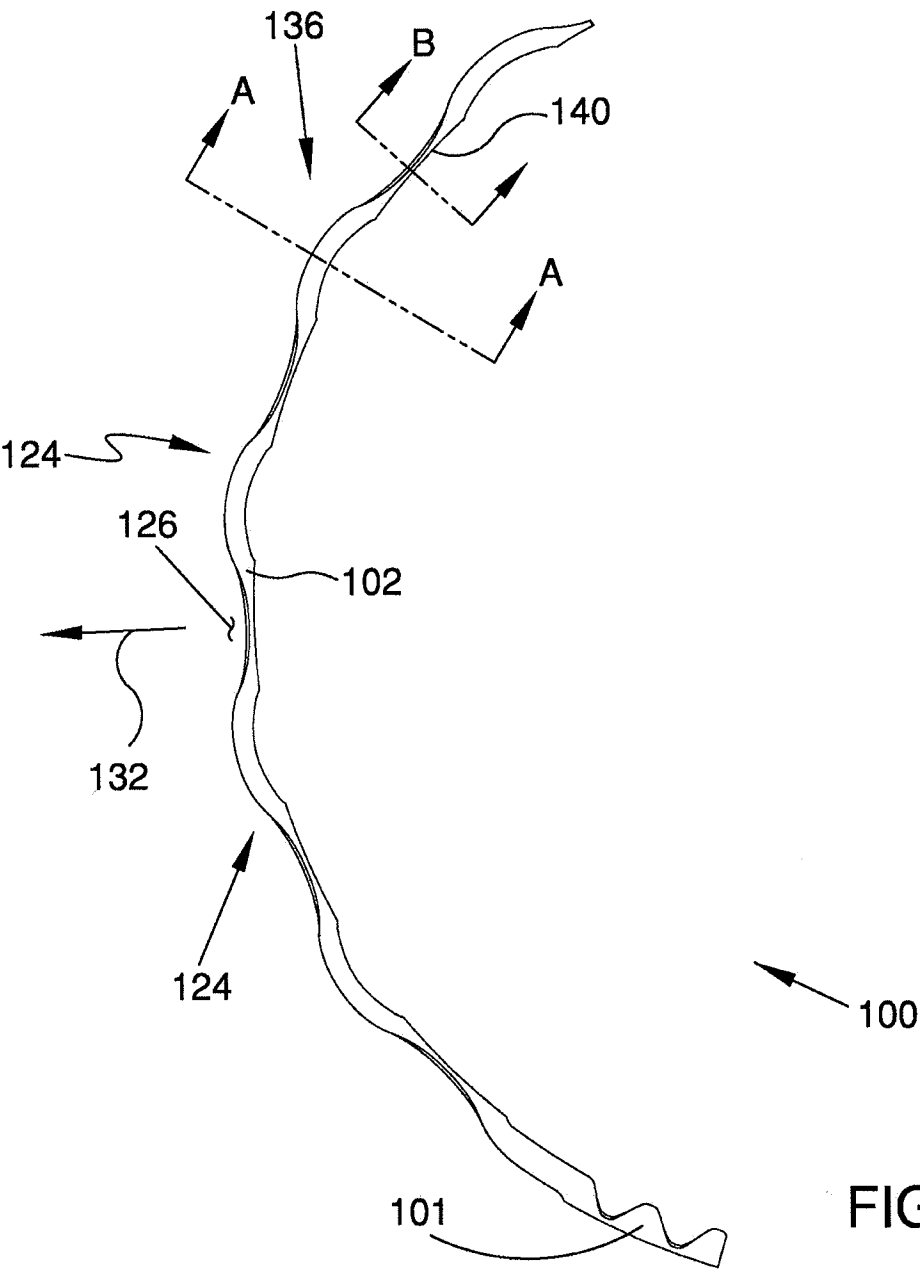
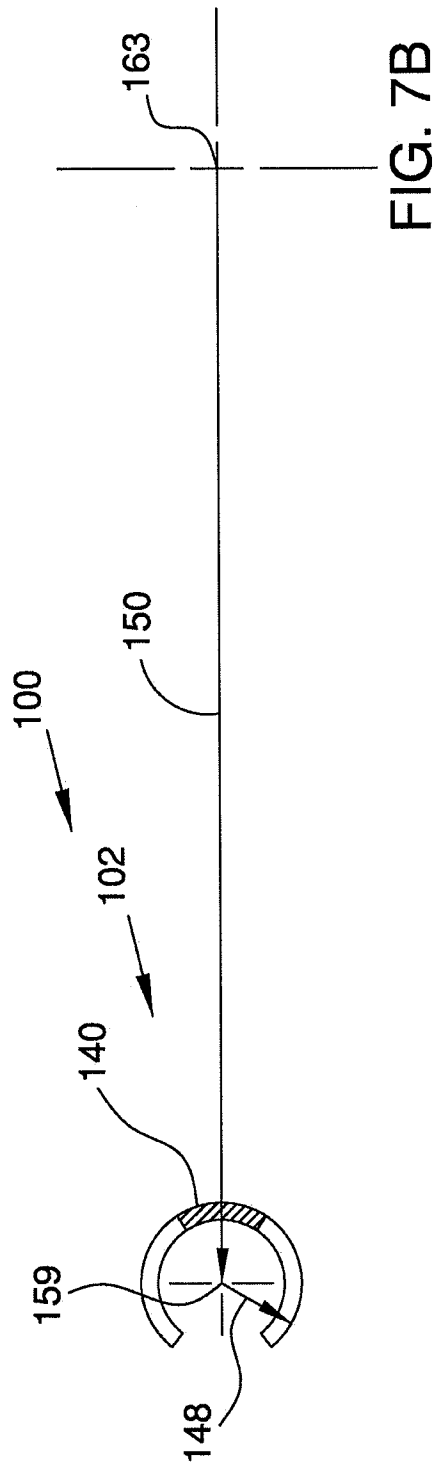
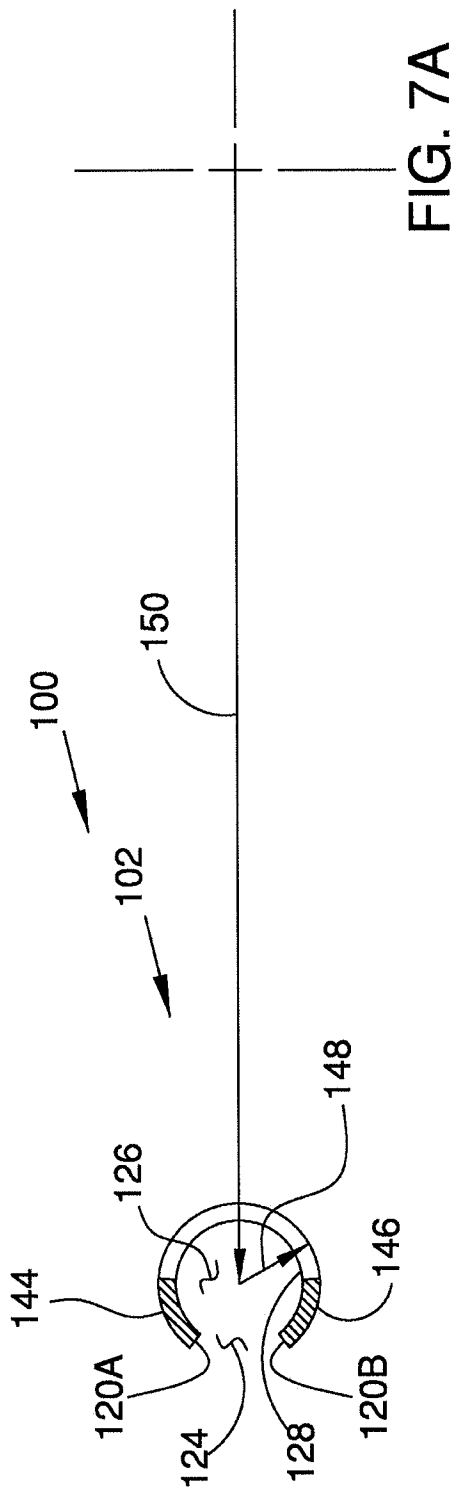
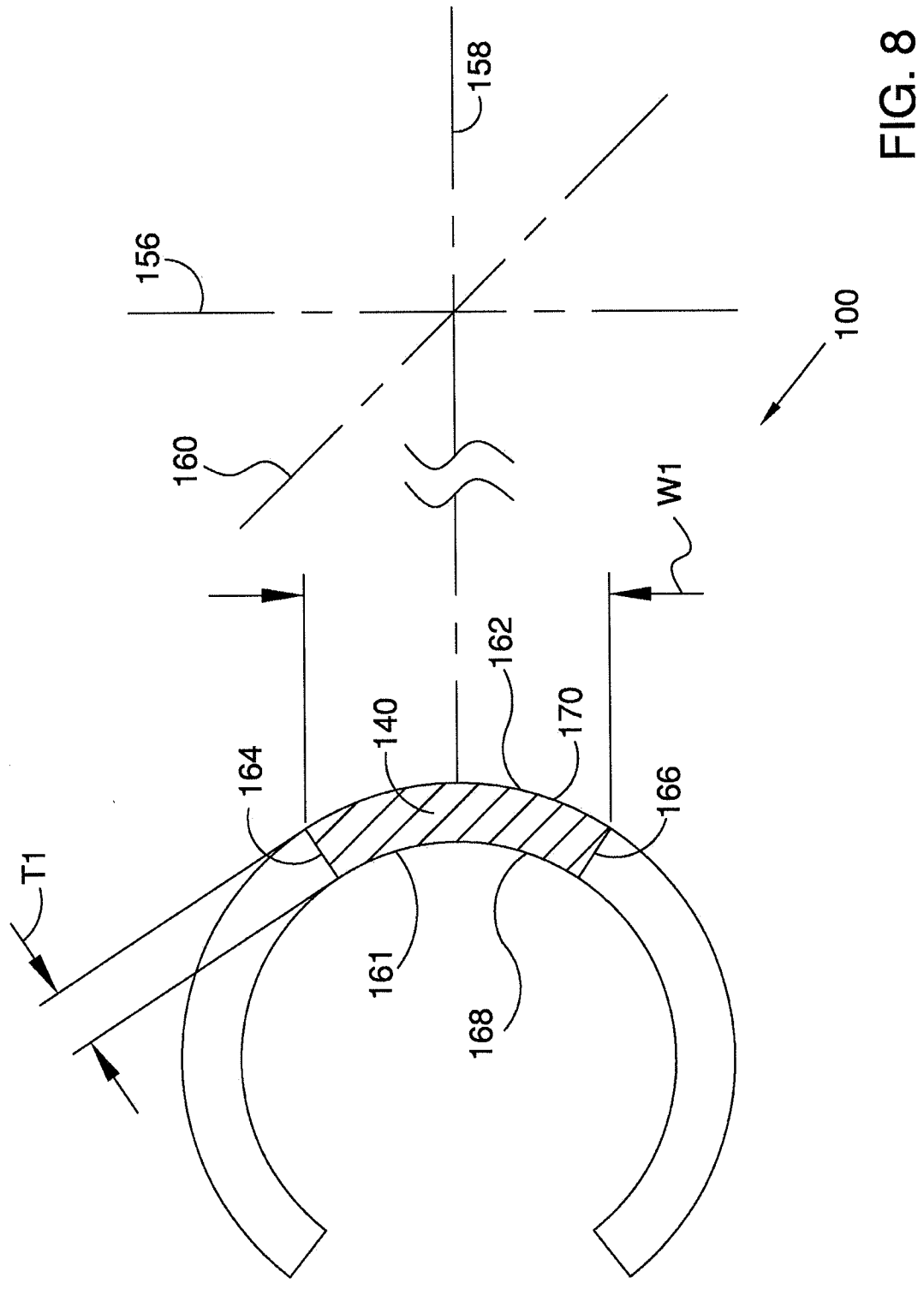
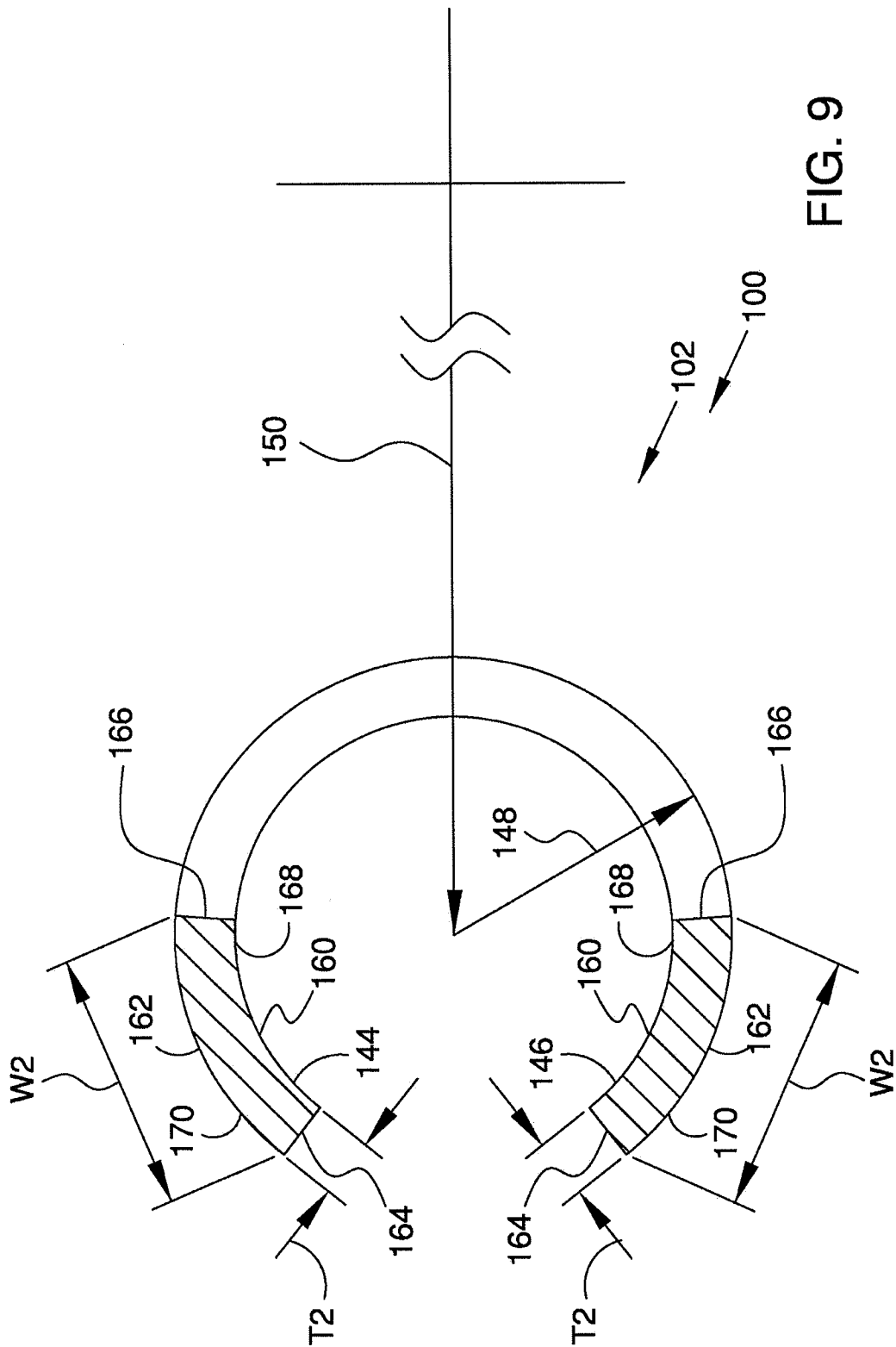


FIG. 6







11 / 35

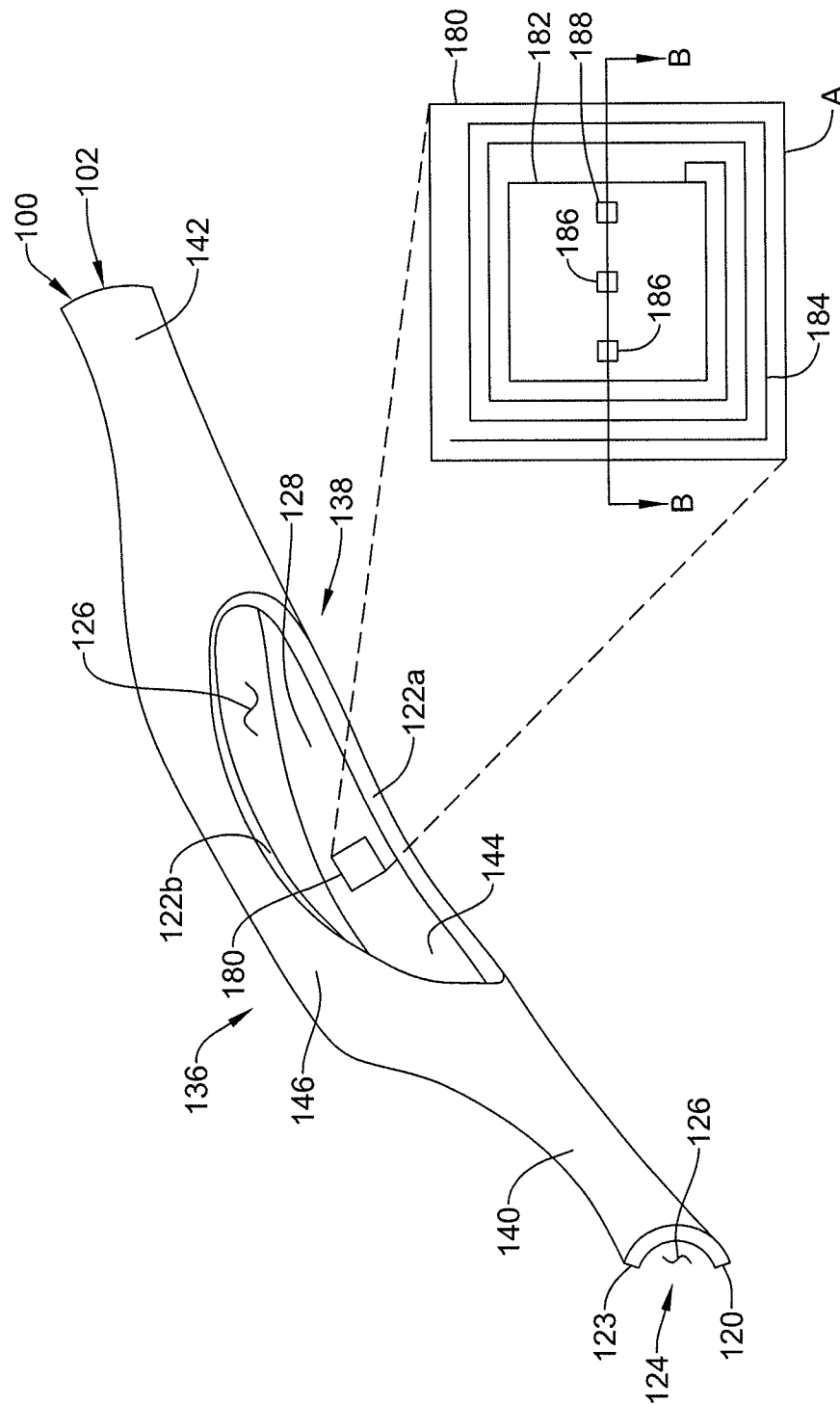


FIG. 10A

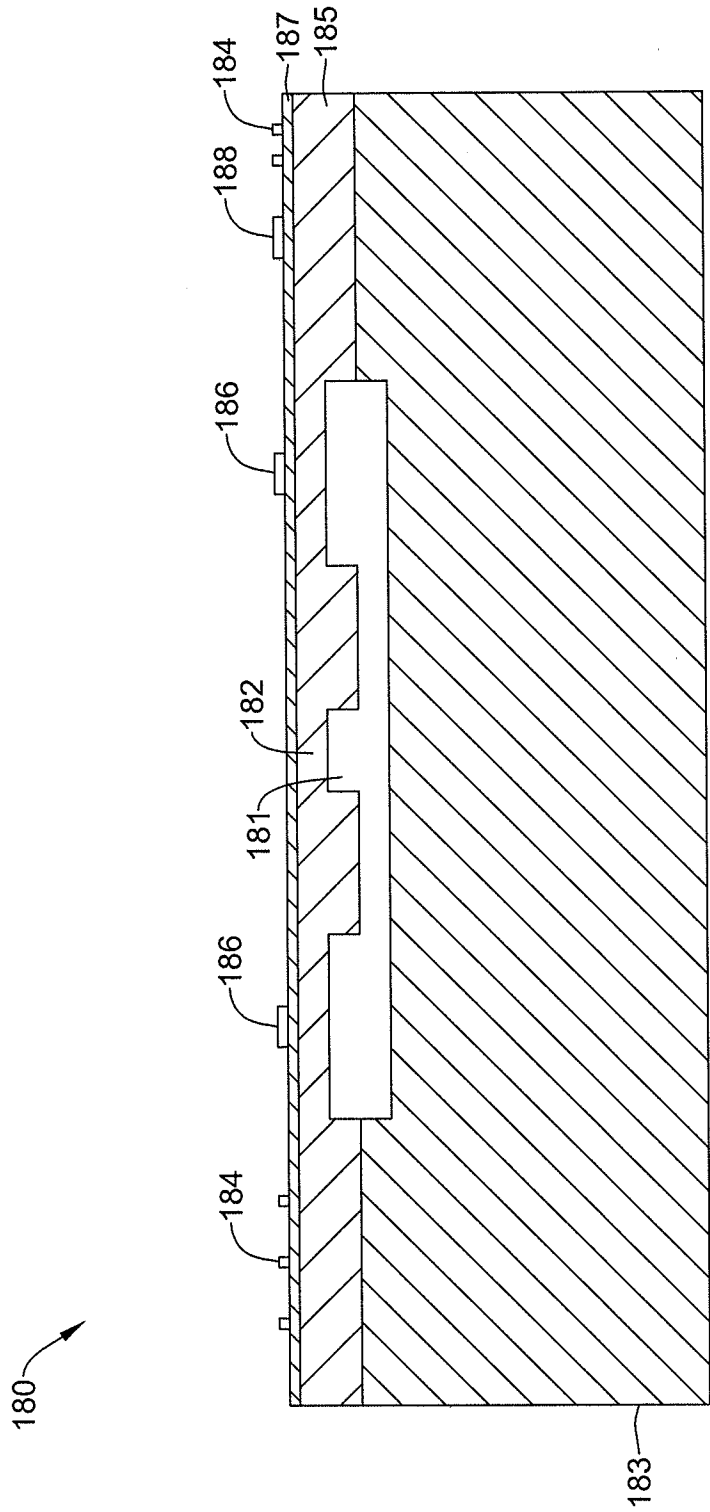


FIG. 10B

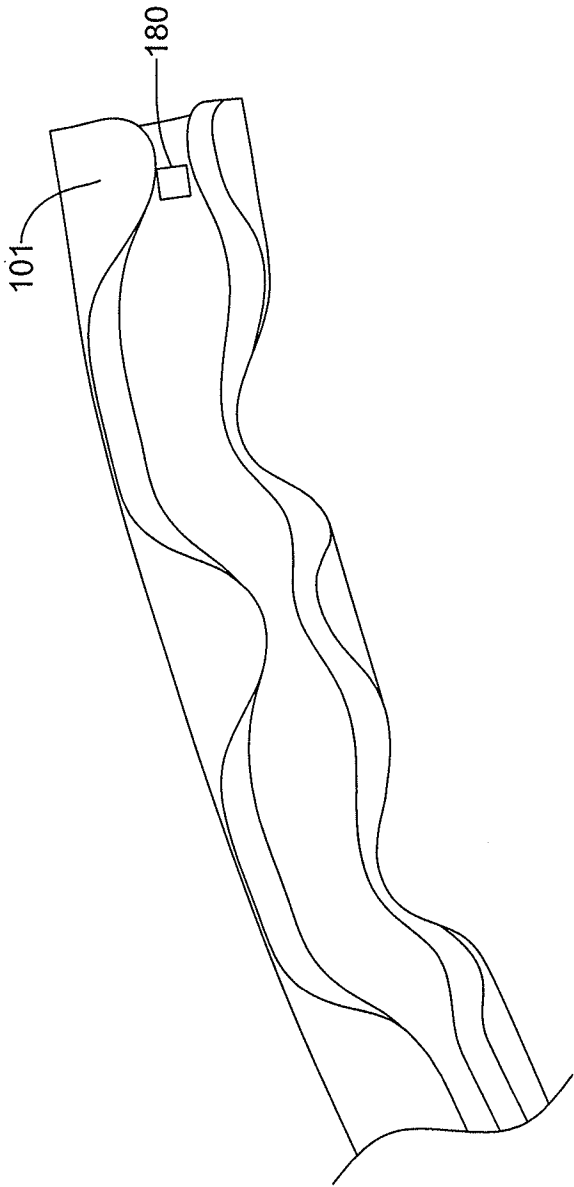


FIG. 10C

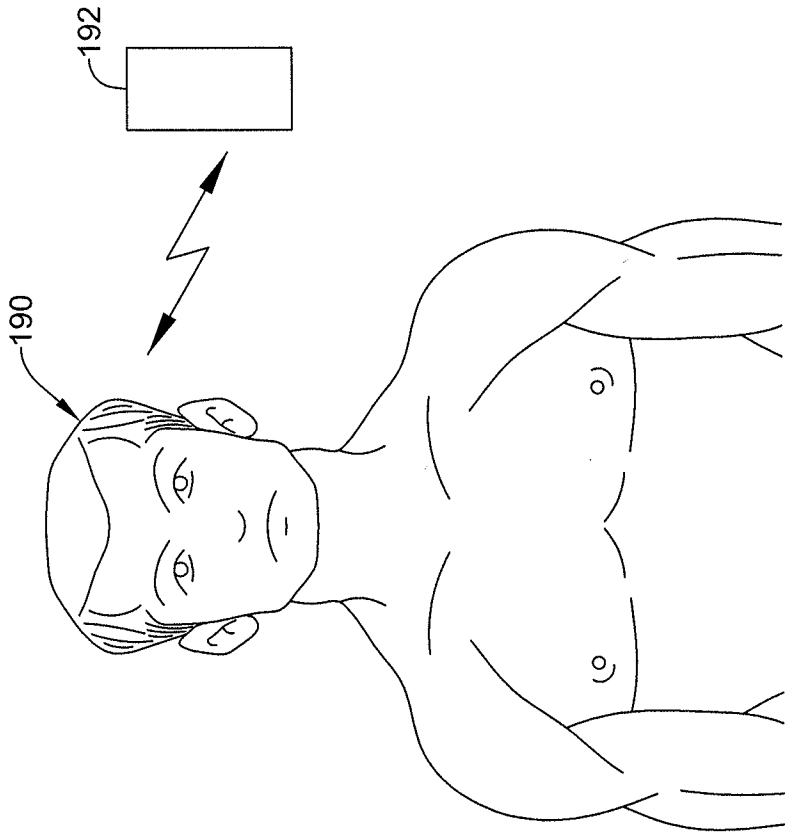


FIG. 11

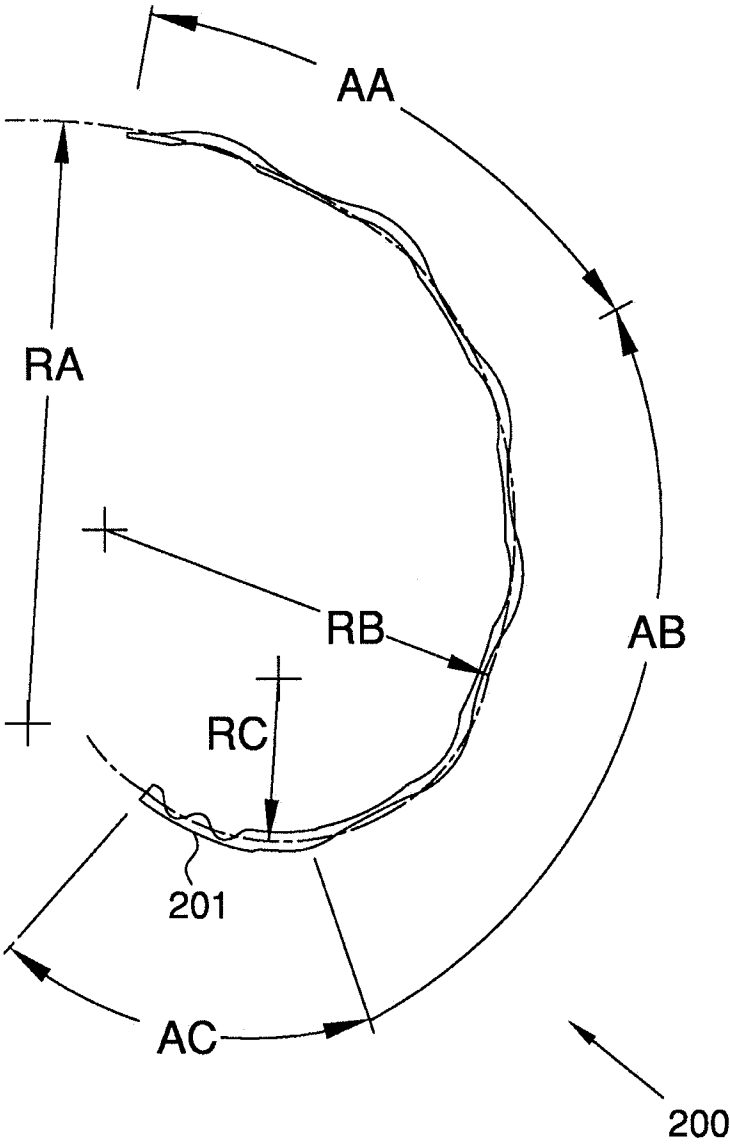


FIG.12

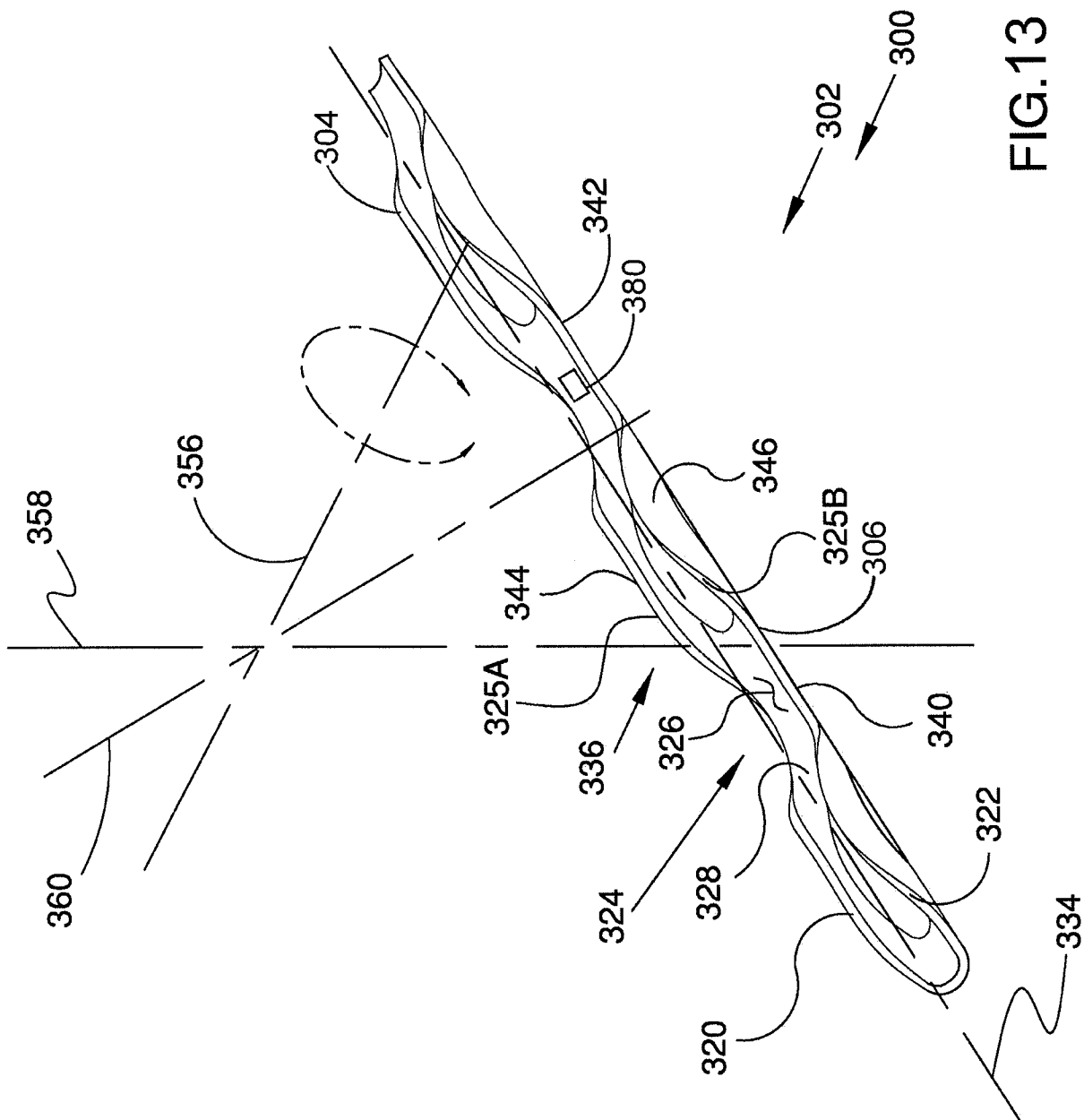
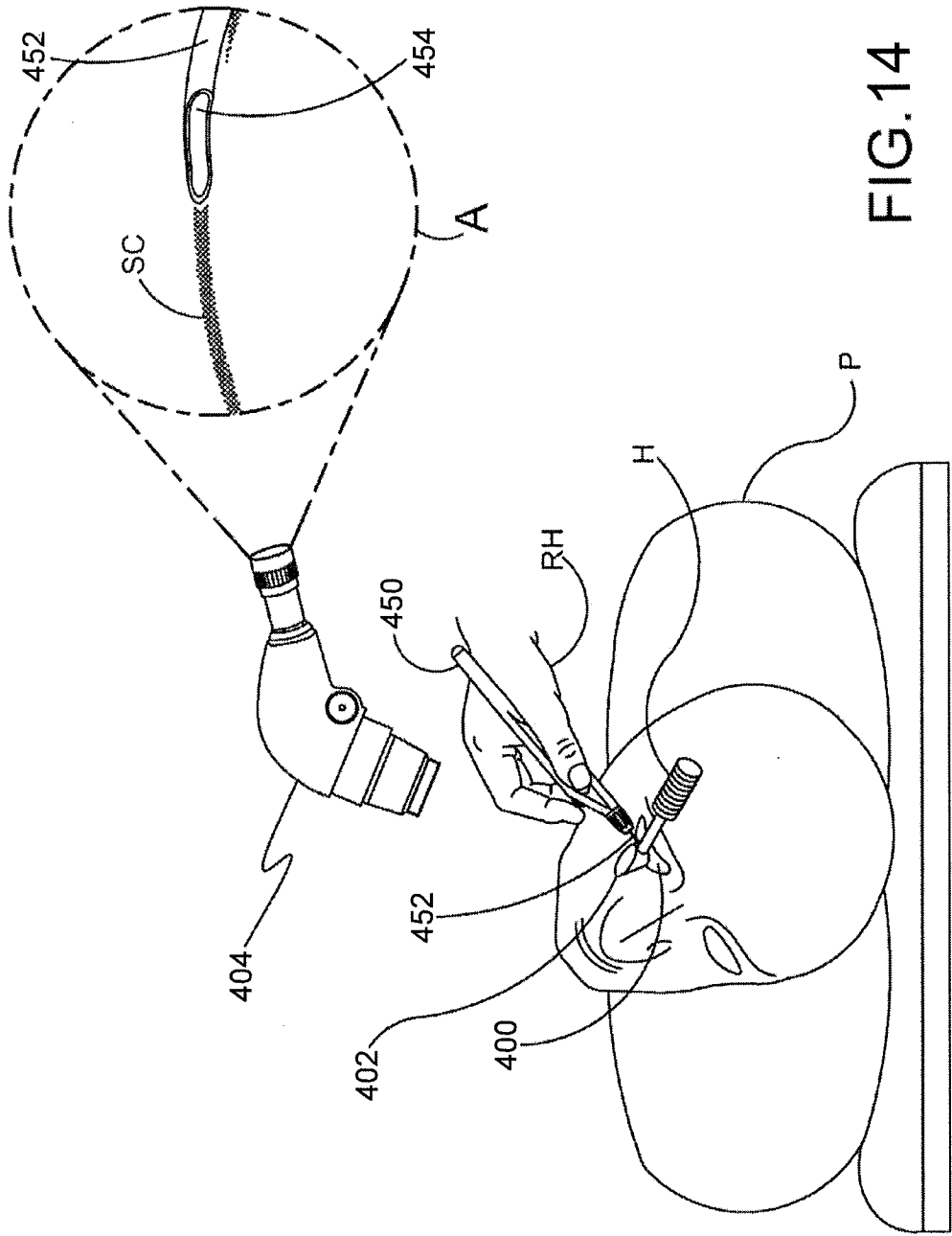


FIG. 13



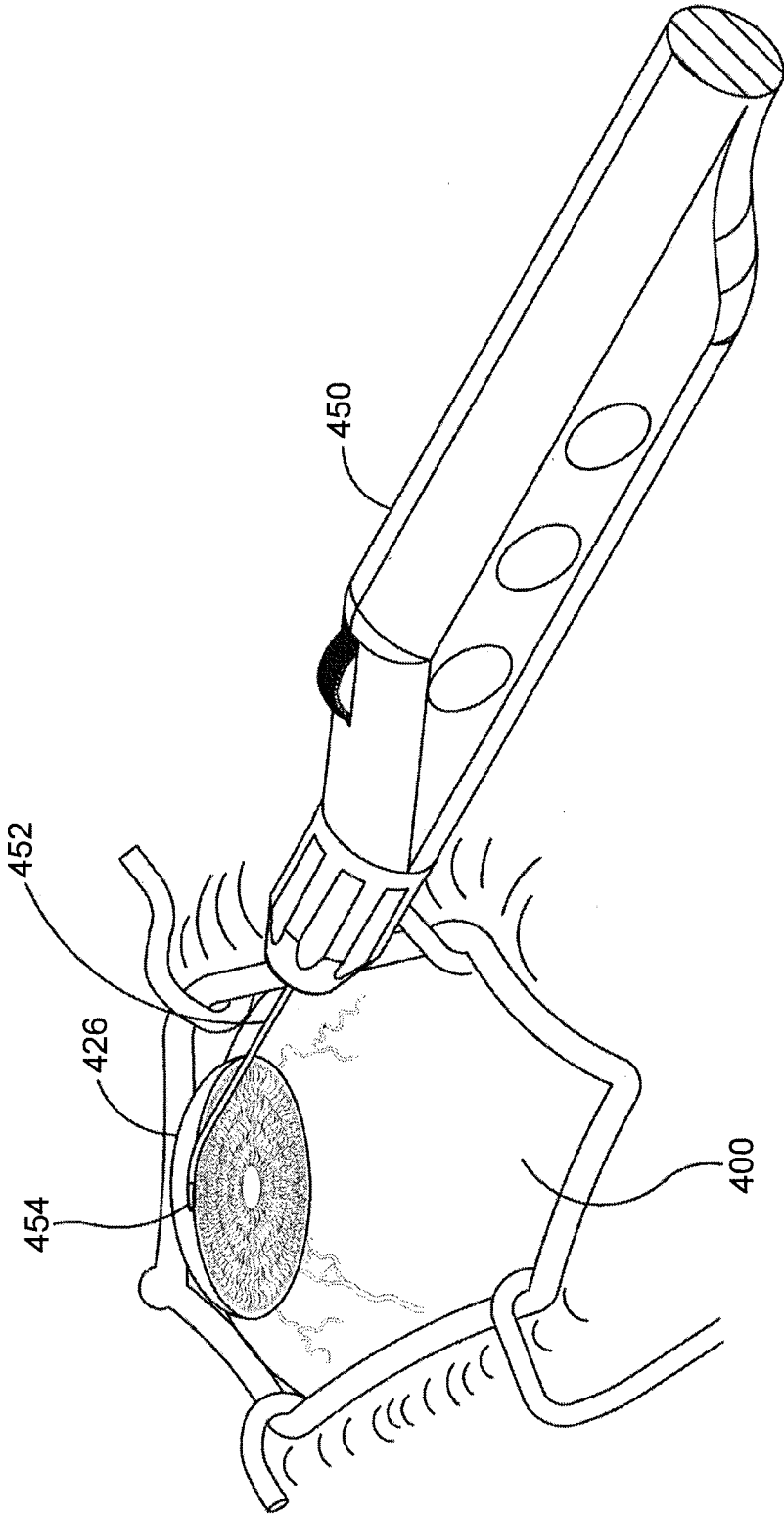
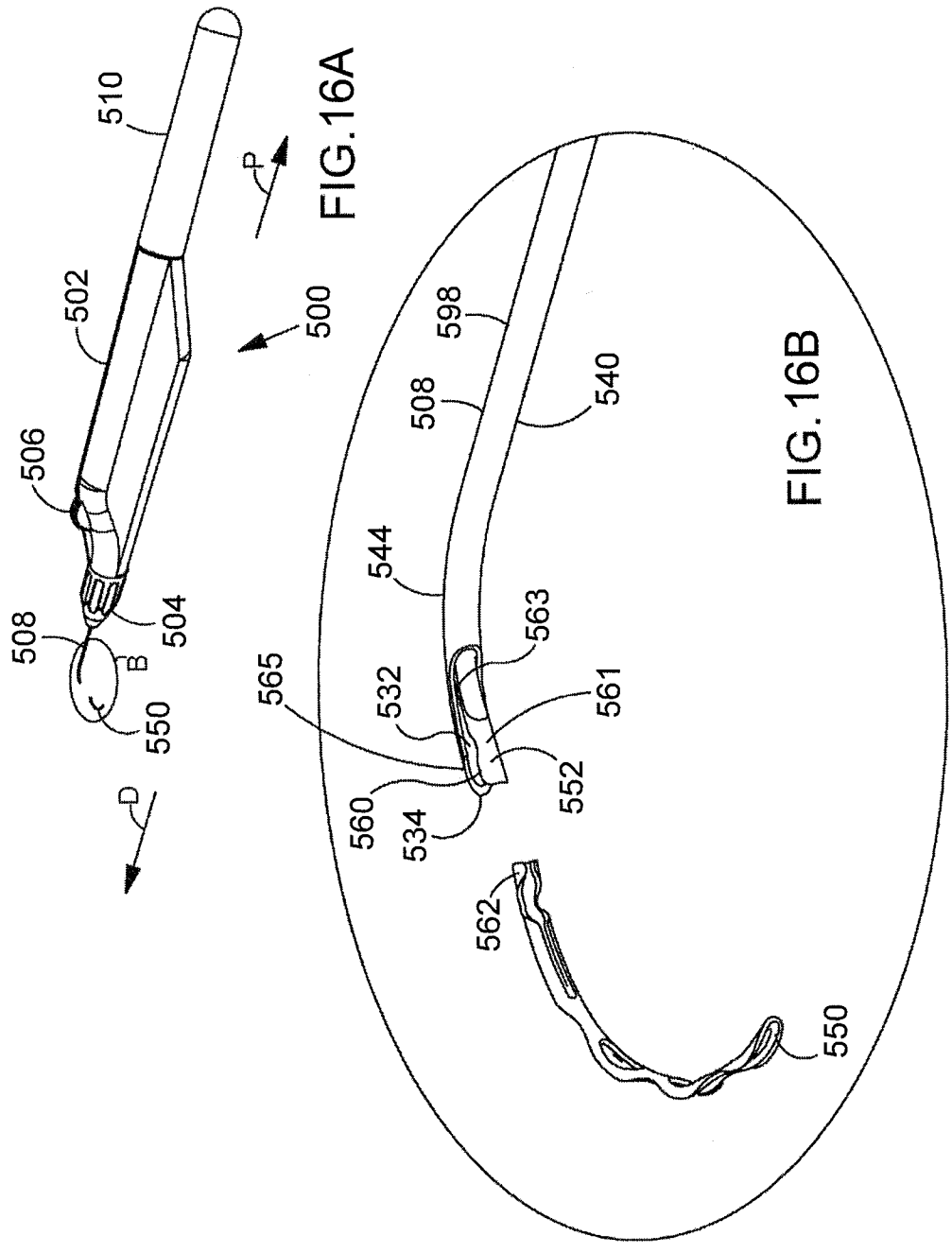


FIG.15



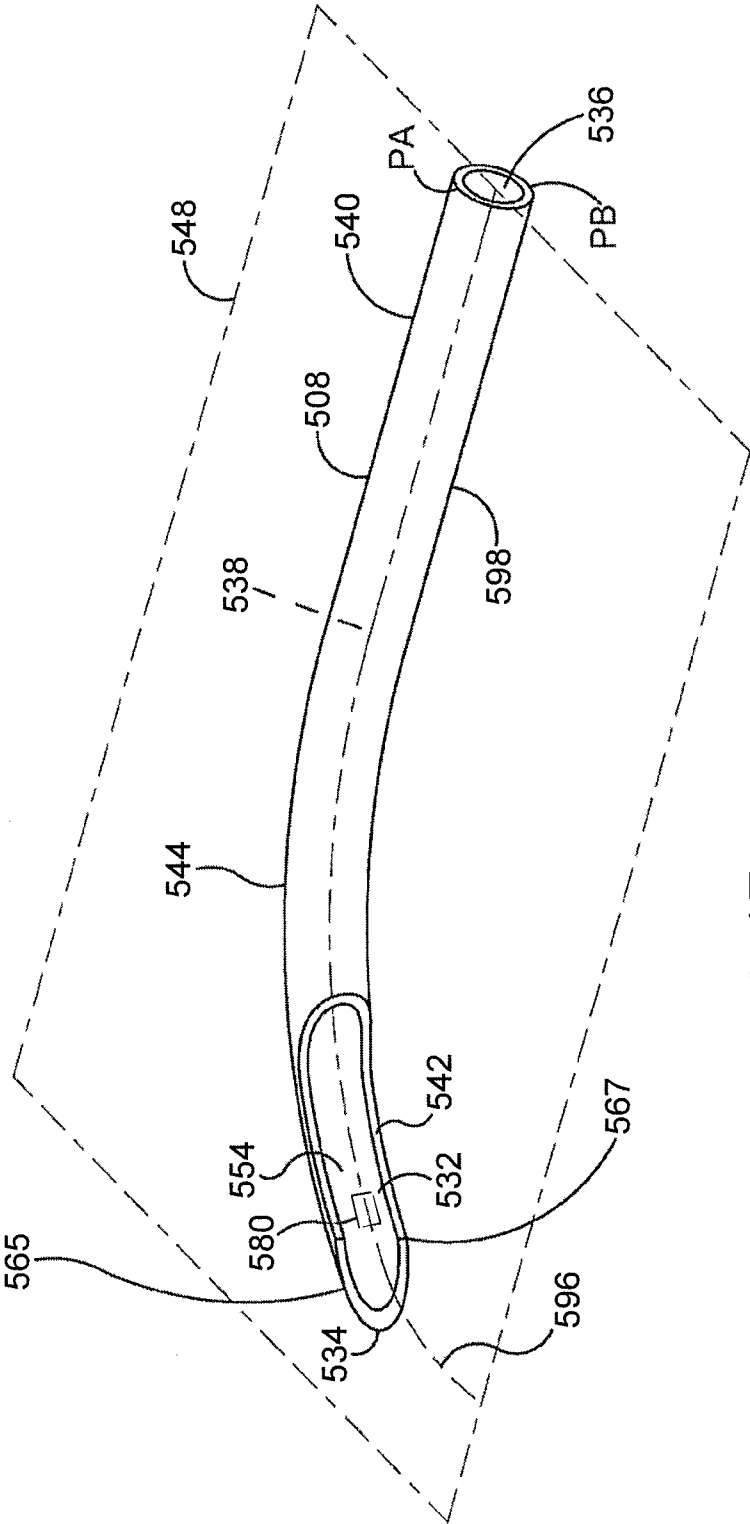


FIG.17

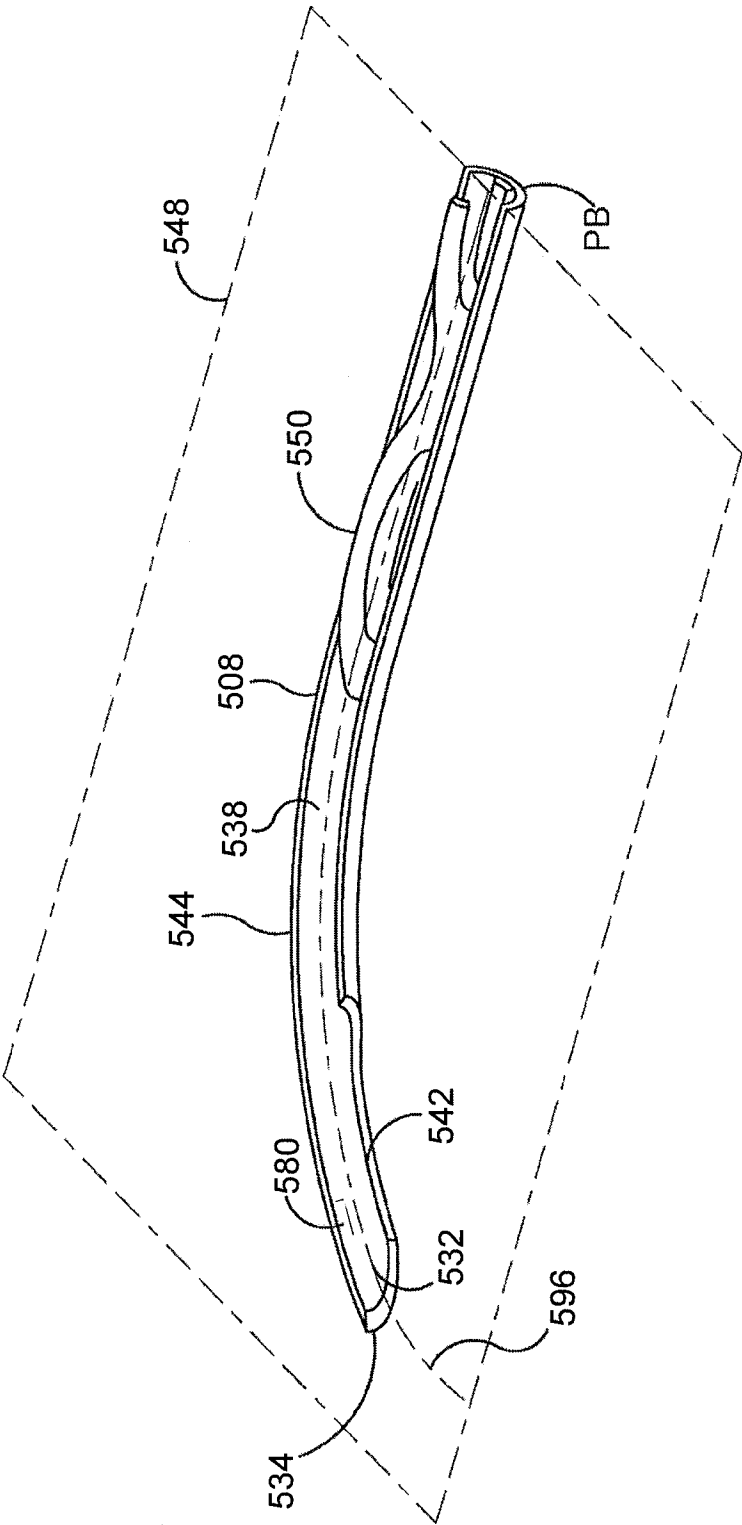


FIG.18

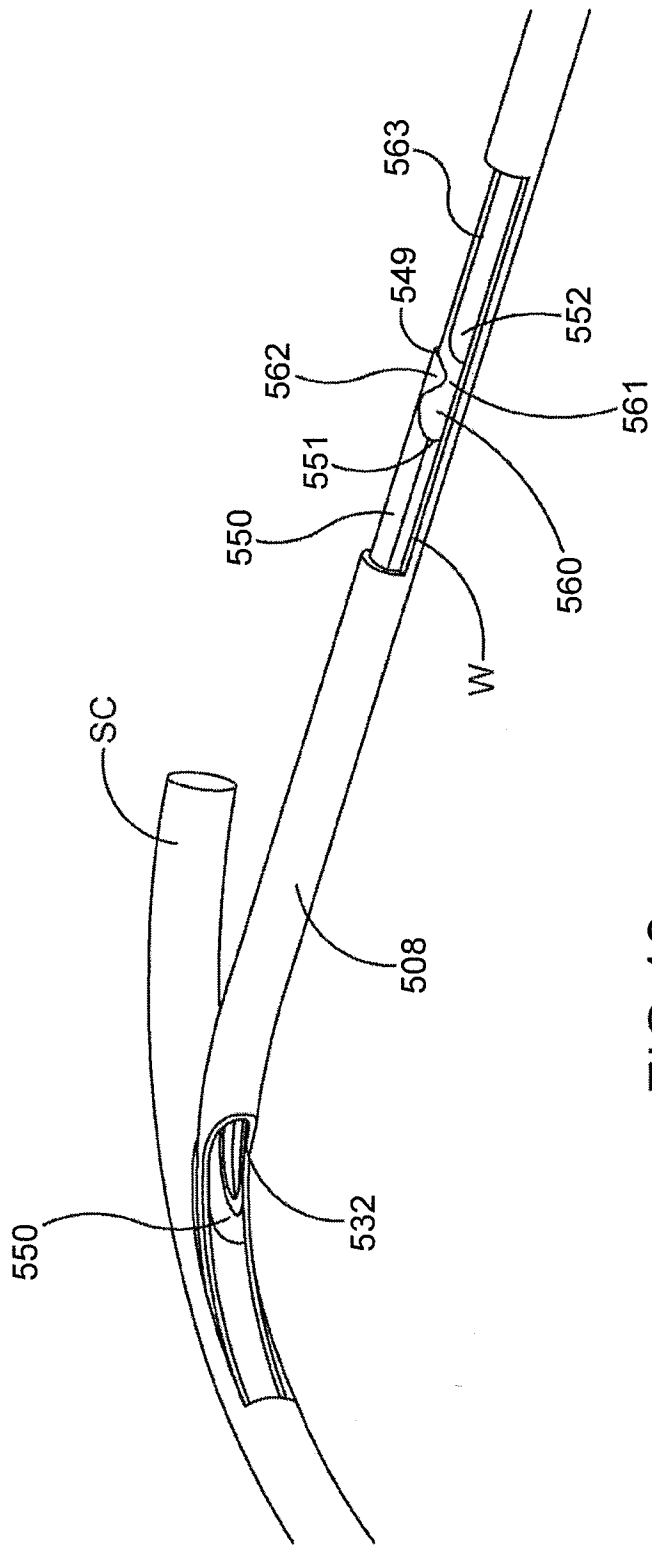


FIG.19

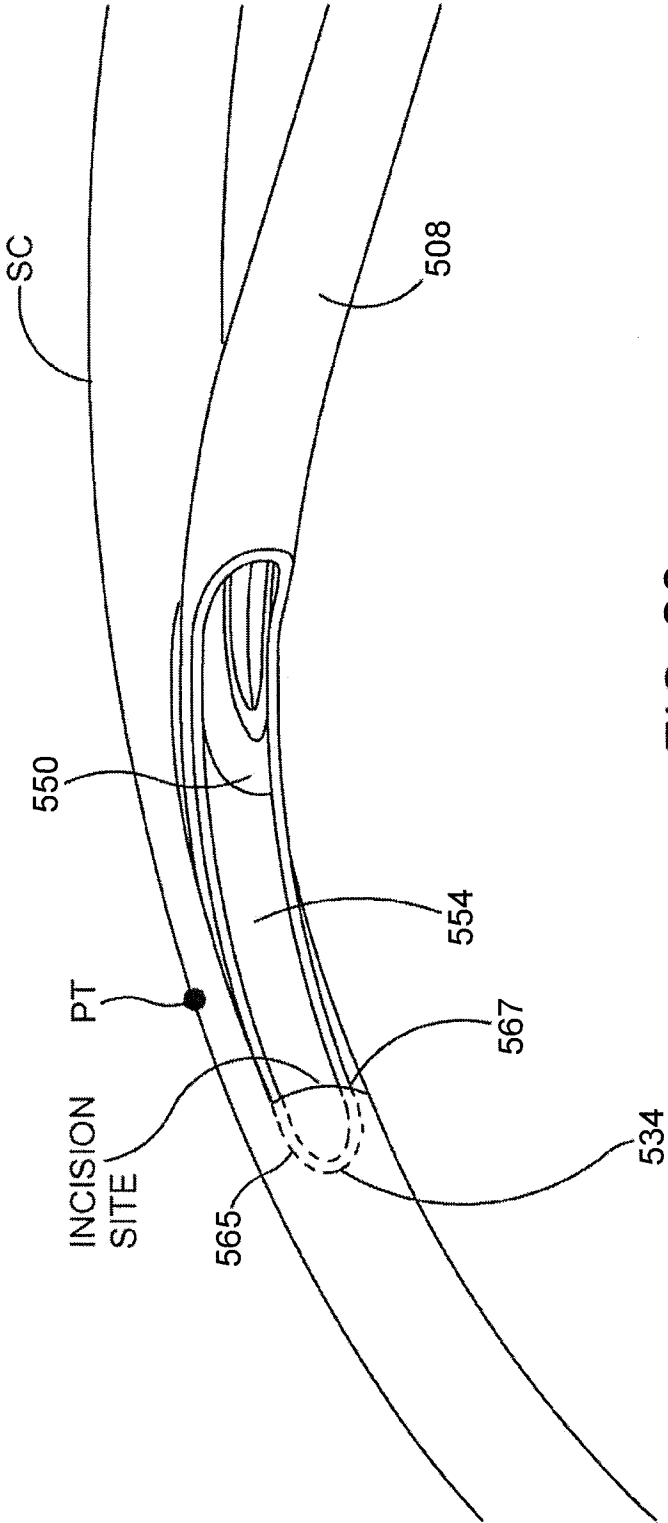


FIG. 20

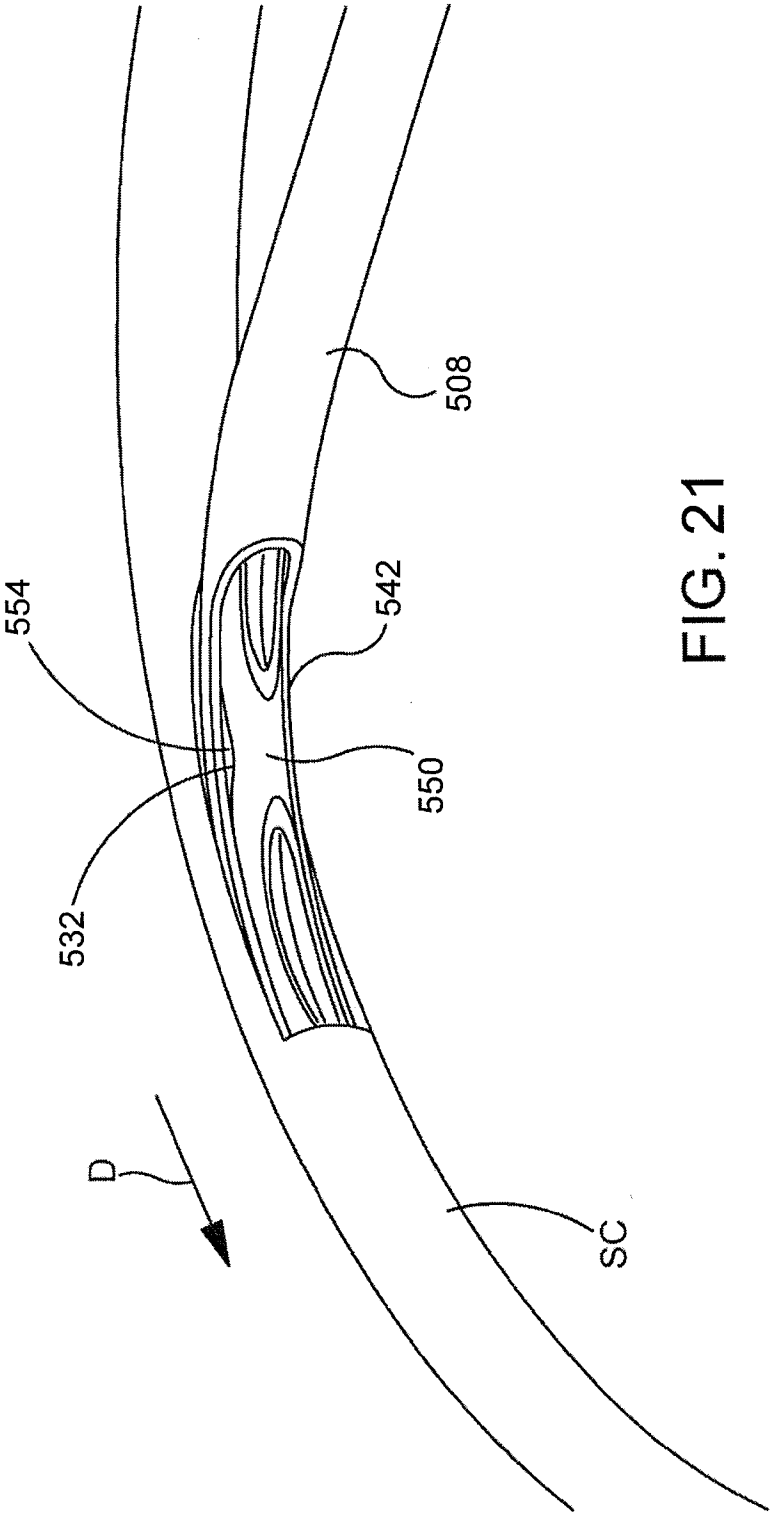


FIG. 21

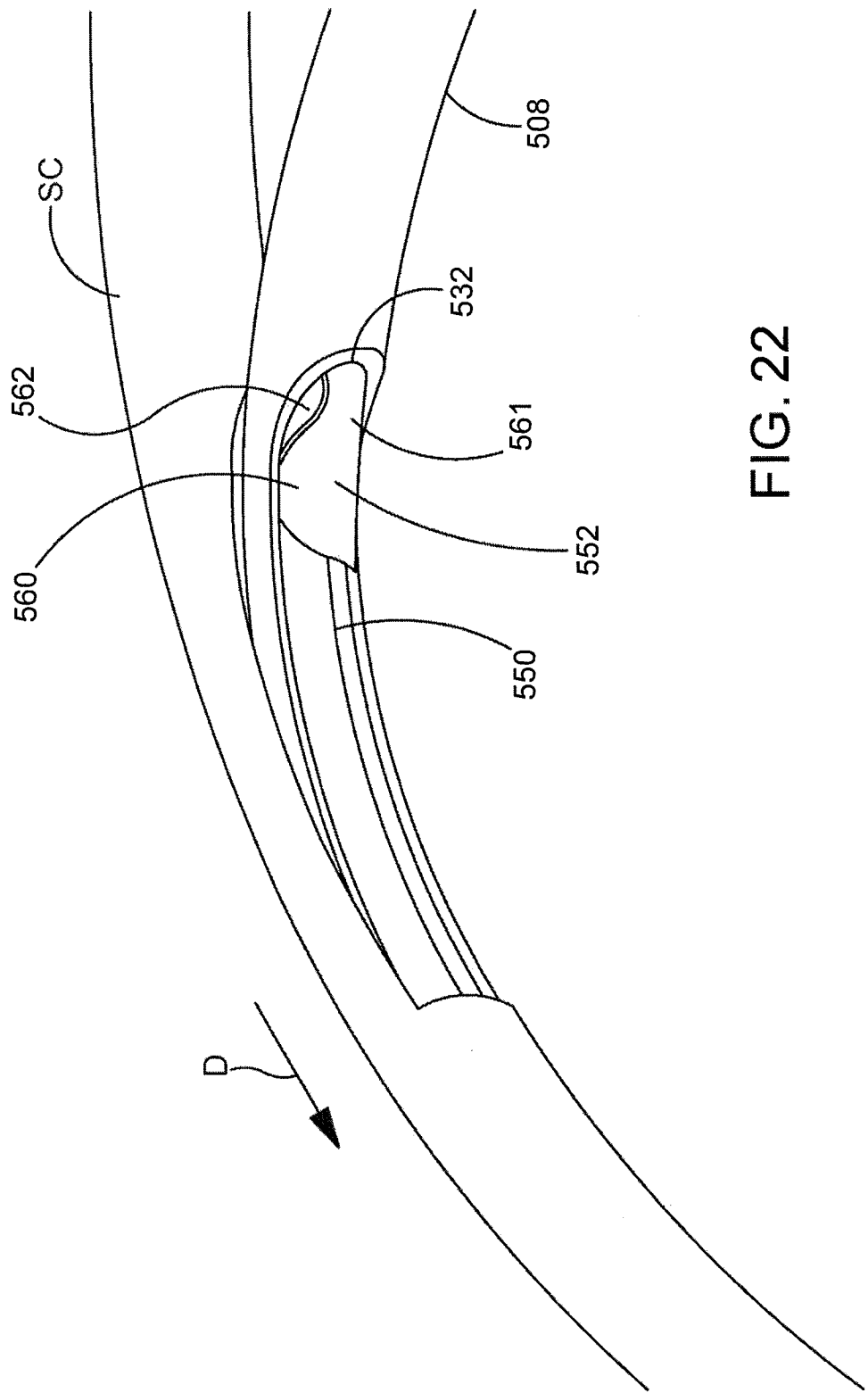


FIG. 22

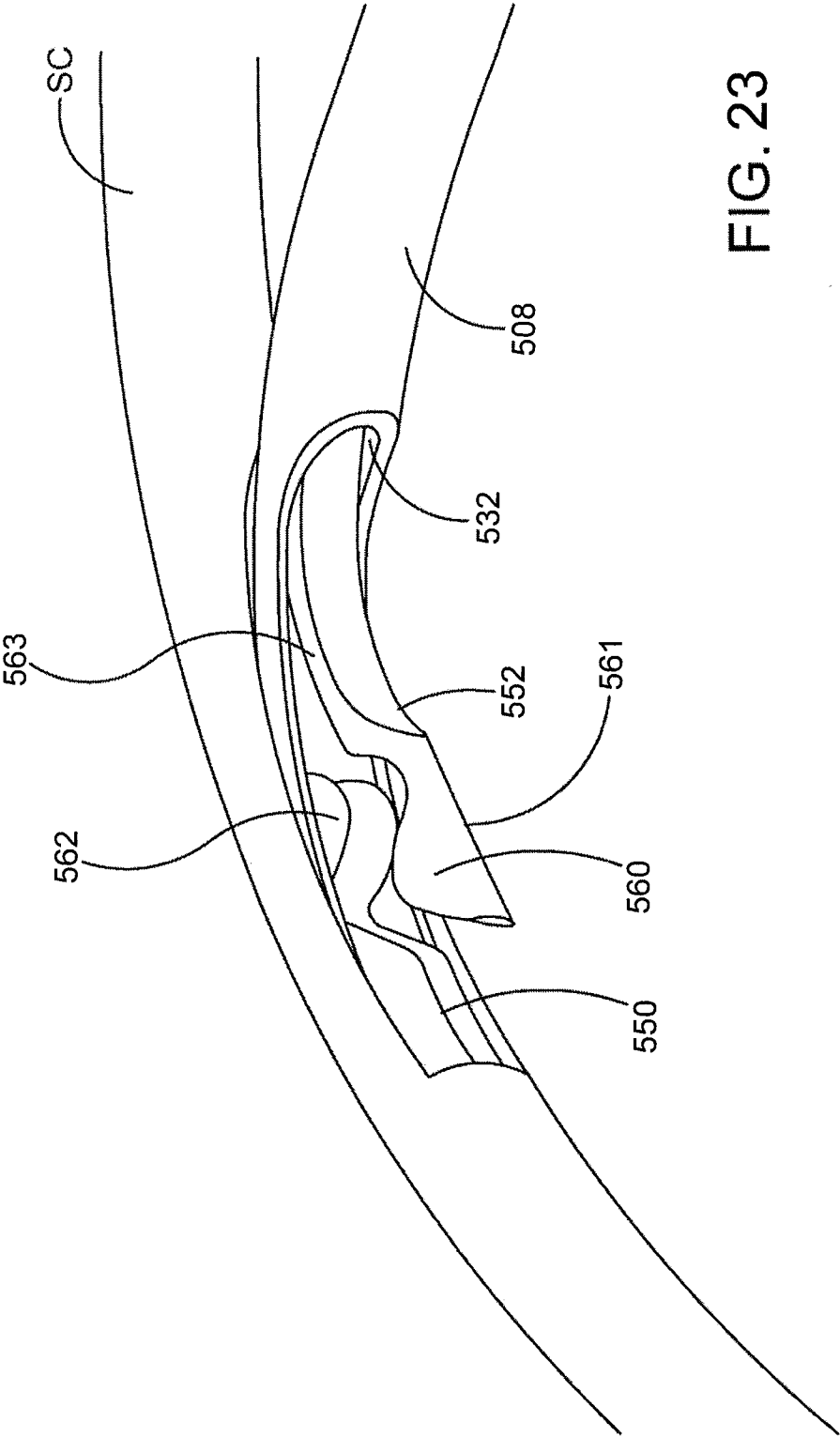


FIG. 23

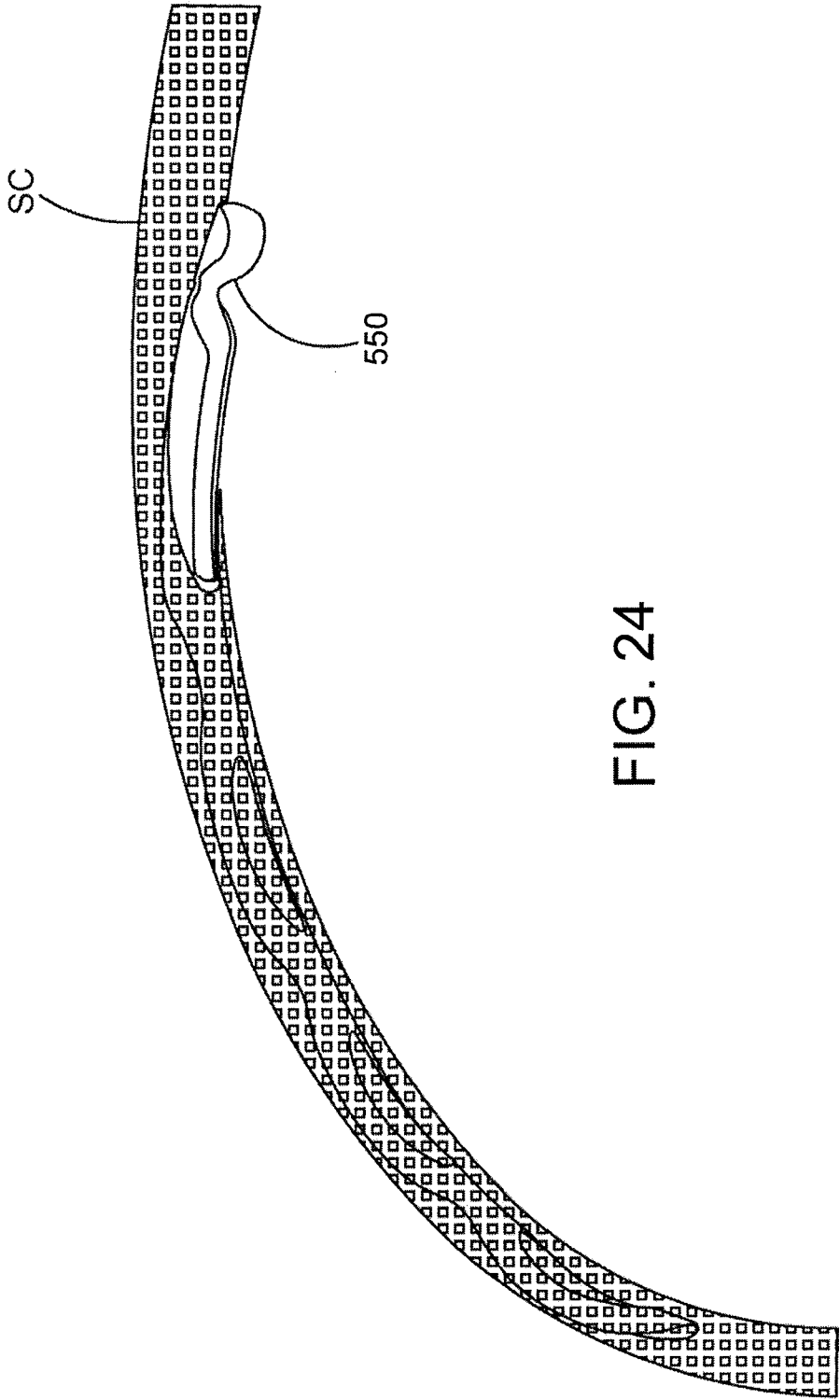


FIG. 25A

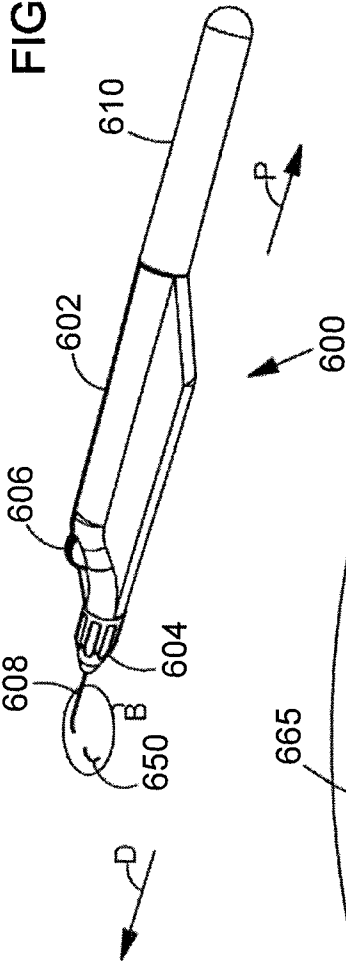
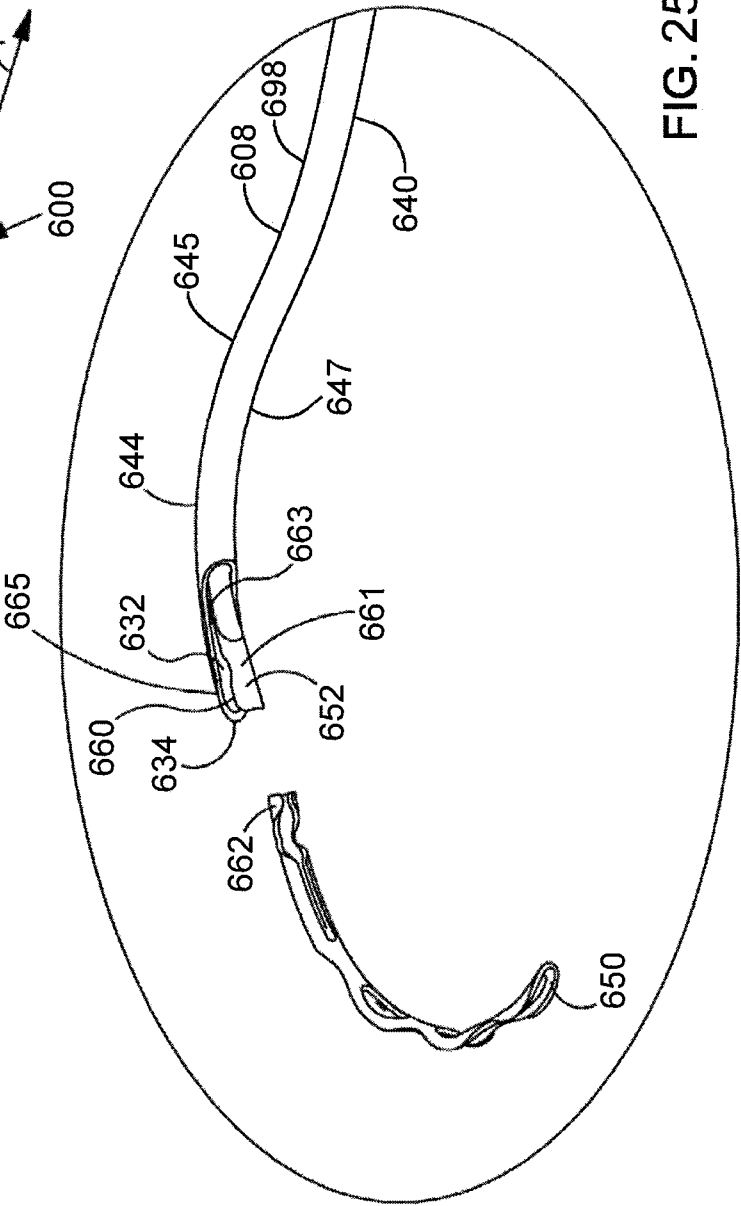


FIG. 25B



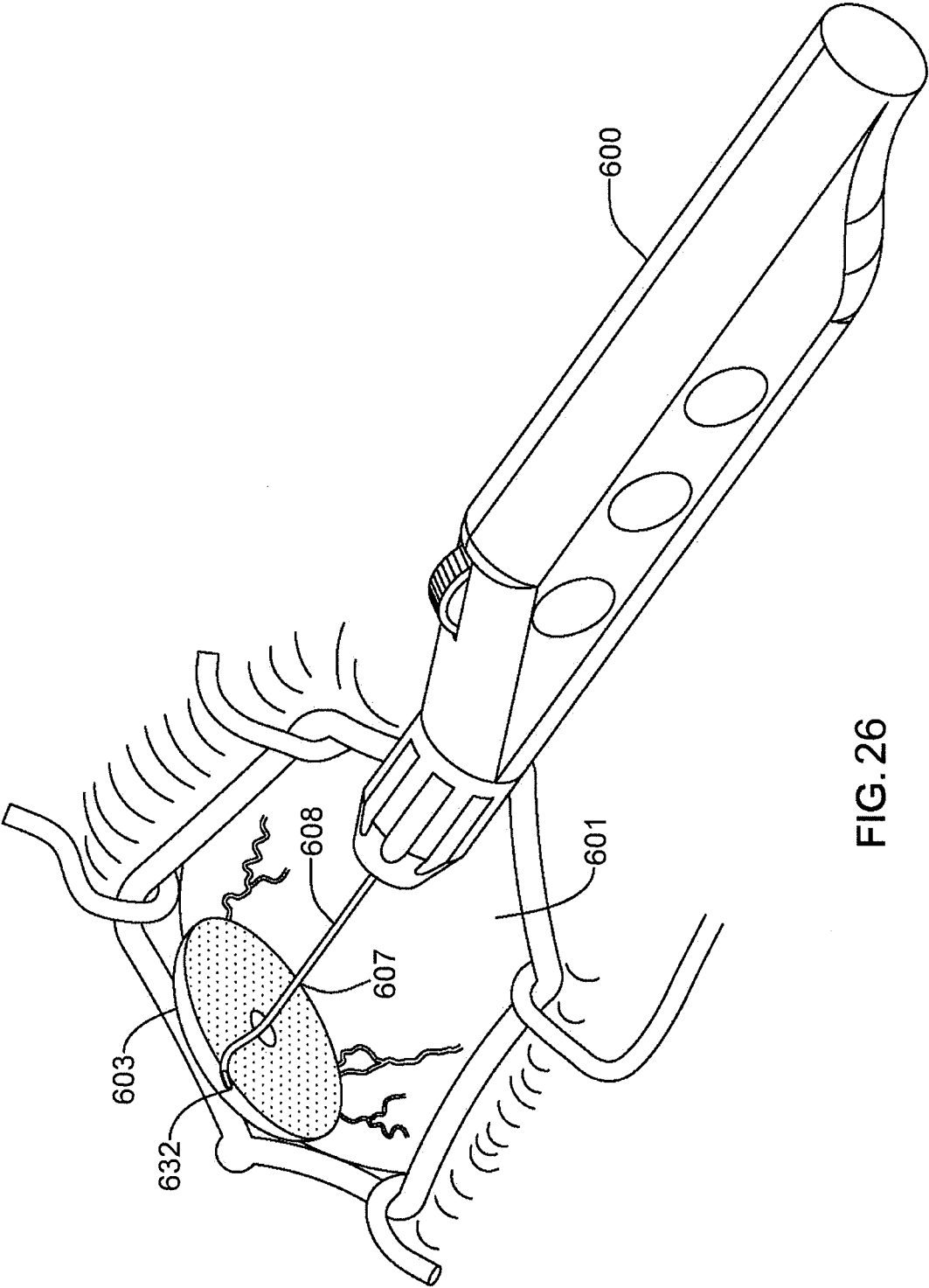
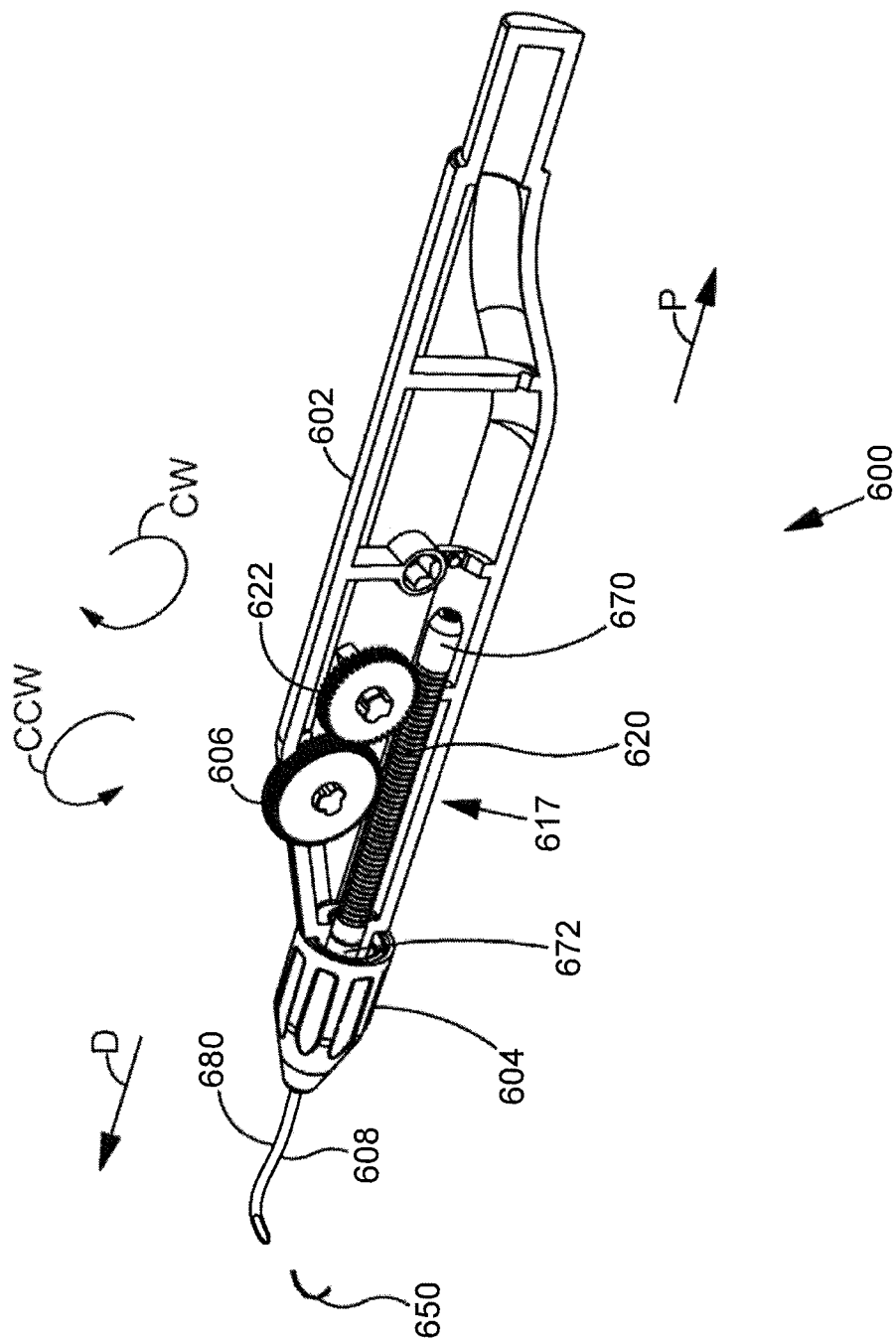


FIG. 26



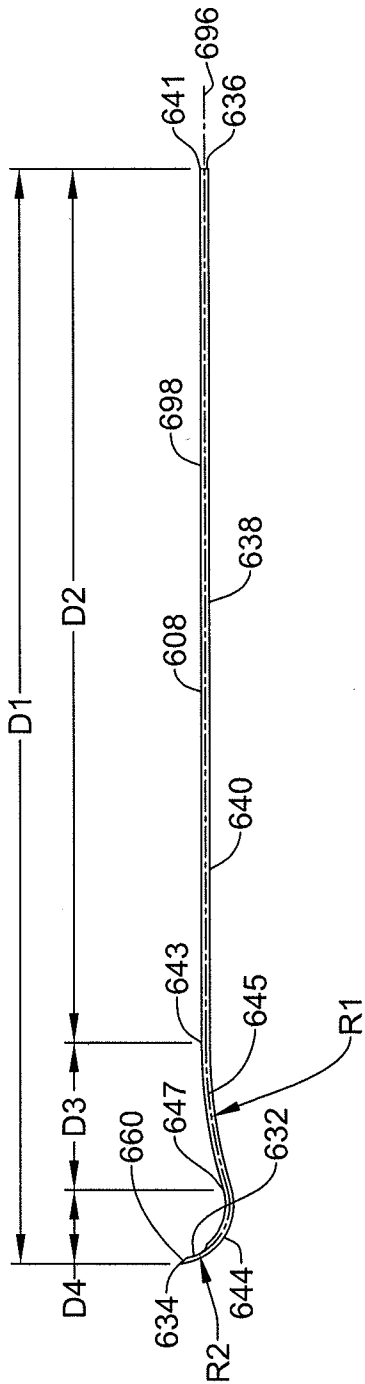


FIG. 28

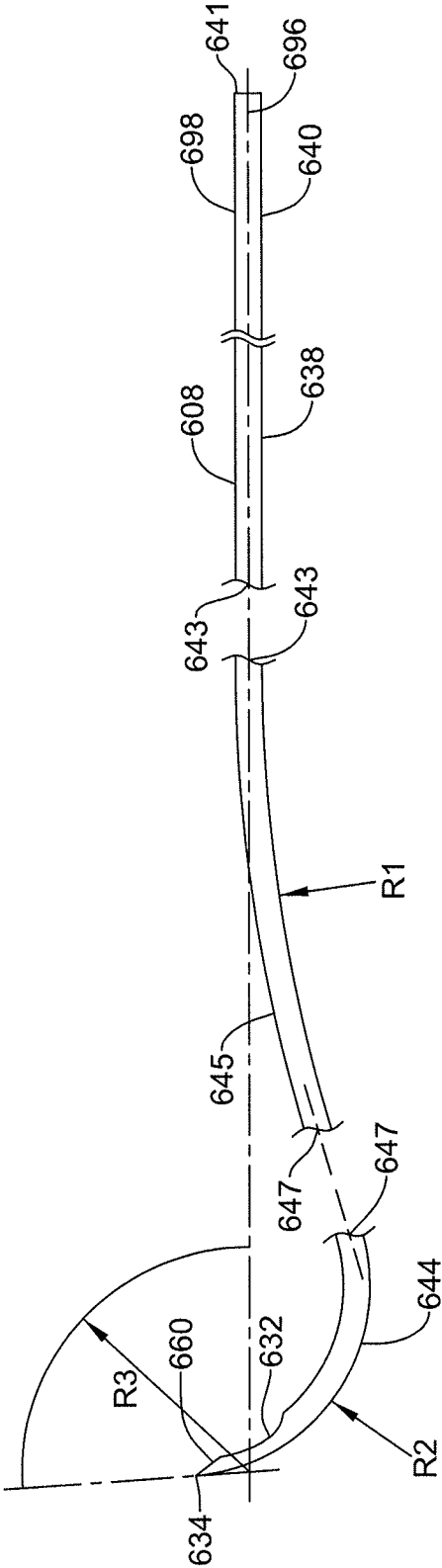


FIG. 28A

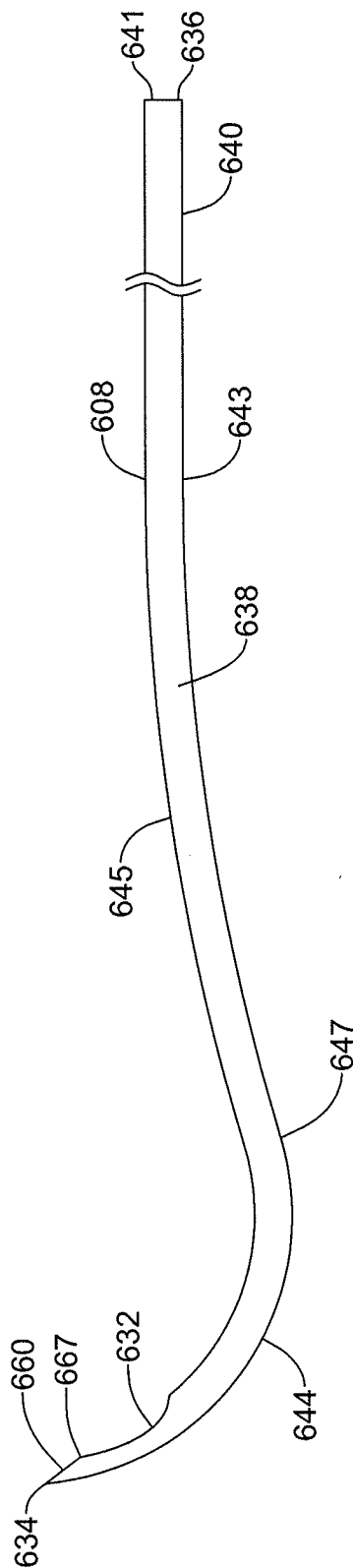


FIG. 29

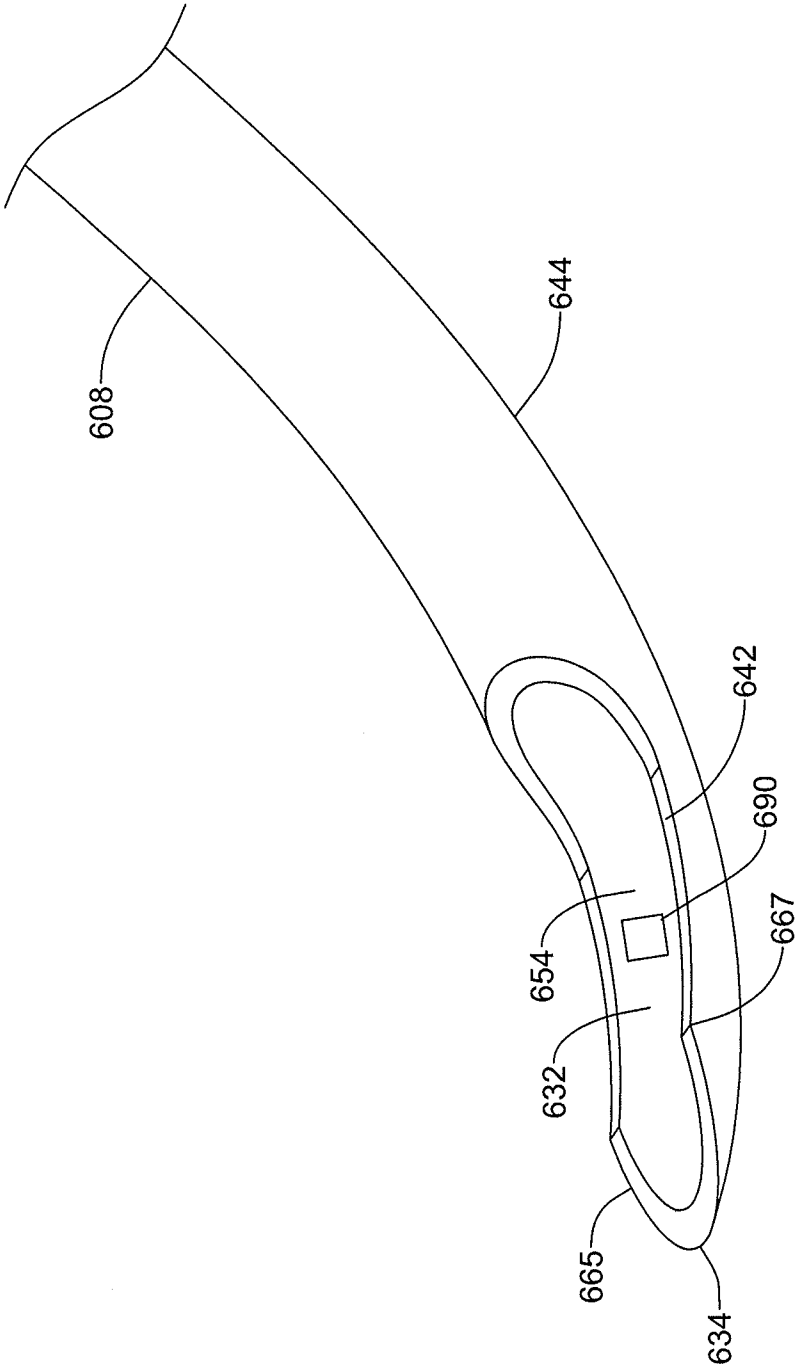


FIG. 30

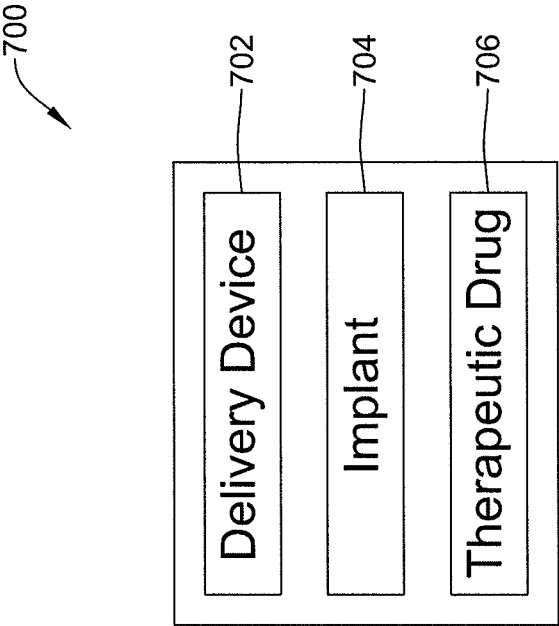


FIG. 31

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 16/66957

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61F 2/16, A61M 5/00, A61F 9/00, A61F 9/007, A61M 25/00, A61M 1/00 (2017.01)

CPC - A61F 9/00781, A61F 2/14, A61M 5/0, A61F 9/0017, A61M 210/0612, A61F 2009/00891 (See Extra Sheet)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 8,529,494 B2 (EUTENEUER et al.) 10 September 2013 (10.09.2013), entire document, Fig. 1, 3A	1-14
Y	US 6,673,812 B1 (AZUMA et al.) 6 January 2004 (06.01.2004), entire document, Figs. 4 and 5, Col. 21, Ins. 29-67; Col. 22, Ins. 1-65	1-14
Y	US 8,529,622 B2 (BADAWI et al.) 10 September 2013 (10.09.2013), entire document, Col. 15, Ins. 53-65	3, 4, 10, 11
Y	US 6,981,958 B1 (GHARIB et al.) 3 January 2006 (03.01.2006), entire document, Col. 11, Ins. 28-38; Claim 1	7, 14
A	US 8,414,518 B2 (SCHEIBER et al.) 9 April 2013 (09.04.2013), entire document	1-14
A	US 8,372,026 B2 (SCHIEBER et al.) 12 February 2013 (12.02.2013), entire document	1-14
A	US 8,287,482 B2 (BADAWI et al.) 16 October 2012 (16.10.2012), entire document	1-14
A	US 2011/0098809 A1 (WARDLE et al.) 28 April 2011 (28.04.2011), entire document	1-14
A	US 8,629,161 B2 (MIZUNO et al.) 14 January 2014 (14.01.2014), entire document	1-14
A	US 8,647,659 B2 (ROBINSON et al.) 11 February 2014 (11.02.2014), entire document	1-14

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

6 February 2017

Date of mailing of the international search report

25 MAY 2017

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 16/66957

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Group I: Claims 1-14, directed to a method for reducing intraocular pressure in a patient, comprising deploying an ocular implant.

Group II: Claims 15-20, directed to a kit for reducing intraocular pressure in a patient, comprising: an ocular implant, a cannula, and a delivery tool.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Claims 1-14

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/66957

Continued from:

A. CLASSIFICATION OF SUBJECT MATTER

CPC: A61F 9/007, A61K 9/0051, A61F 2009/00885

According to International Patent Classification (IPC) or to both national classification and IPC

EXHIBIT G

REFINITIV STREETEVENTS

EDITED TRANSCRIPT

Alcon AG at JPMorgan Healthcare Conference (Virtual)

EVENT DATE/TIME: JANUARY 12, 2022 / 4:15PM GMT

JANUARY 12, 2022 / 4:15PM GMT, Alcon AG at JPMorgan Healthcare Conference (Virtual)

real advantage to taking new technology into the market.

So let me pass to the next slide and just comment a little bit on our [Ivantis] integration. We're very pleased to report that we closed the integration this last week, and we added the Hydrus Microstent into our portfolio. This is a \$60 million starting point on a \$500 million market that we didn't participate in. Now ever since we withdrew CyPass, this was a market that we've always had a very high interest in. It's a market growing in the low teens and a market that we think has tremendous potential to grow further.

I think what's important about this idea that people may want to understand is that our timing really couldn't have been better. The 5-year pivotal data that Ivantis took on some time ago is the longest continuous follow-up of a MIG device. And what it's demonstrated are some really fundamentally important ideas for the MIG space. First and foremost, this 5-year data talks about safety. It's a very safe product. But secondly, what it says is that 65% of patients who at 5 years, had the MIG in their eye, had [hydrus] in their eye, they were medication-free. That's a tremendous amount of cost savings and a tremendous amount of quality of life, and it's never been shown at that distance in that definitive in nature.

The second thing is that, that same group of patients, 60% less likely to have a follow-on surgery. That means a filtering surgery, a trabeculectomy, something else that is going to cost money and cause quality-of-life damage. So again, the savings associated with this product and inserting this product are being established in a long-term, important randomized clinical trial.

And maybe most interesting, the [Moorfields] folks out in London have shown on the same set of data that we can slow the progression of glaucoma in these patients by almost half. So if you understand that to be in essence, a patient that could go blind in 10 years now goes blind in 20 years, that is a remarkable product, and those are the kinds of things that we think expand the market. What it does is it creates an environment where reimbursement becomes much more obvious. The argument for reimbursement becomes more obvious and the need and the desire to put these in with that kind of data, we think, given our footprint around the world and our opportunity to bring this data to market creates a unique opportunity for us. So we're excited about what's going on there. We're really pleased and proud of what the Ivantis team has done over there.

Now moving on to the Slide 11. Let me just comment a little bit on the long-term view of cataract surgery. One of the things that we're very aware of is that the cataract surgeons in the United States in particular, but around the world, are not going to be sufficient to do the amount of surgery that's coming through the system. So it is imperative that the efficiency of surgery improves. So the demand for surgery is going to continue to go up. Number of surgeons in the U.S. is not keeping pace. And the demand for AT-IOLs in particular is also going up. So what we know that means is we've got to get better efficiency. That means faster surgeries, safer surgeries, we've got to lower cost and we've got to improve outcomes. And so as we think about that, the kind of critical idea is to unify the whole of the cataract surgery into an ecosystem of equipment that works together in a very efficient manner.

Let me tell you what I mean. Today, the patient comes into the pre-op environment in the office and probably sits through 5 or so different exams that takes a couple of hours that most of that information is taken off in paper, put into the chart that's also paper, stacked into 20 other charts that goes to the surgical planner. The Surgical Planner then, whether it's a doctor or a surgical assistant, inputs that data into a calculator on the computer. They make a plan for the surgery. They put it back in the folder. They put it over here on this right side. They do that 20 times if it's 20 surgeries the next day. That's an incredibly inefficient process. But then they go to the OR and they take each one of those pieces and they load that data, they move the data on the landmarking information into the OR and they proceed with their surgery. They come back. They take the post-op measurements, they do the same thing again.

We believe there's a huge opportunity to streamline that. There's probably 35% of that, that can come out of that system by allowing the equipment to work with the cloud planner that we've invented now and got into the market this last AAO. The Smart Cataract planner for us will accept data from any instrument in the office. But in particular, we have a new ARGOS biometer we'll talk about that moves that data into the cloud. Now that automatically transfers the information there. More information transfers in. The surgeon can then plan wherever she wants to be if she's at home, if she's on the road, if it's the night late. It's an opportunity to plan from any location you want and do the things that need to be done for next-day surgery. When you get there, all that information is pulled down for the cloud by the Phaco machine onto the visualization system. So it's all available for you in a heads-up cockpit that looks like a surgical setting from what you'd expect.

EXHIBIT H

TESS was last updated on Wed Jun 8 03:32:23 EDT 2022

TESS HOME

NEW USER

STRUCTURED

FREE FORM

BROWSE DICT

SEARCH OG

BOTTOM

HELP

PREV LIST

CURR LIST

NEXT LIST

FIRST DOC

PREV DOC

NEXT DOC

LAST DOC

Logout

Please logout when you are done to release system resources allocated for you.

Start

List At: OR

Jump


 to record: **Record 35 out of 988**

TSDR

ASSIGN Status

TTAB Status

(Use the "Back" button of the Internet Browser to return to TESS)



Word Mark

Goods and Services

Mark Drawing Code

Serial Number

Filing Date

Current Basis

Original Filing Basis

Published for Opposition

Owner

Attorney of Record

Priority Date

Prior Registrations

Description of Mark

Type of Mark

Register

Live/Dead Indicator

ALCON

IC 035. US 100 101 102. G & S: Business management; business administration for others; providing office functions. FIRST USE: 20190630. FIRST USE IN COMMERCE: 20190630

IC 037. US 100 103 106. G & S: Repair of surgical equipment; installation of surgical equipment. FIRST USE: 20190630. FIRST USE IN COMMERCE: 20190630

IC 041. US 100 101 107. G & S: Educational services, namely, conducting classes, seminars, conferences, and workshops in the field of vision care; training services in the field of ophthalmology; organizing exhibitions for cultural purposes. FIRST USE: 20190630. FIRST USE IN COMMERCE: 20190630

(5) WORDS, LETTERS, AND/OR NUMBERS IN STYLIZED FORM

88981445

April 9, 2019

1B

1B;44D

February 18, 2020

(APPLICANT) Alcon Inc. CORPORATION SWITZERLAND Rue Louis-d'Affry 6 Fribourg SWITZERLAND CH-1701

Nancy Sabarra

February 4, 2019

0581463;1055870;1740936

The color blue is claimed as a feature of the mark. The mark consists of the word "**ALCON**" in stylized letters and in the color blue.

SERVICE MARK

PRINCIPAL

LIVE

TESS HOME

NEW USER

STRUCTURED

FREE FORM

BROWSE DICT

SEARCH OG

Top

HELP

PREV LIST

CURR LIST

NEXT LIST

FIRST DOC

PREV DOC

NEXT DOC

LAST DOC

EXHIBIT I

TESS was last updated on Wed Jun 8 03:32:23 EDT 2022

TESS HOME

NEW USER

STRUCTURED

FREE FORM

BROWSE DICT

SEARCH OG

BOTTOM

HELP

PREV LIST

CURR LIST

NEXT LIST

FIRST DOC

PREV DOC

NEXT DOC

LAST DOC

Logout

Please logout when you are done to release system resources allocated for you.

Start

List At: OR

Jump


 to record: **Record 36 out of 988**

TSDR

ASSIGN Status

TTAB Status

(Use the "Back" button of the Internet Browser to return to TESS)



Word Mark

Goods and Services

ALCON

IC 005. US 005 006 018 044 046 051 052. G & S: Ophthalmic preparations; pharmaceutical preparations for the external treatment of hay fever; contrast media used intravenously as an aid to visualize abnormal conditions in the body and as a means of determining circulation time in the blood; contact lens wetting and soaking solutions; a mixture of water soluble polymers sold as an ingredient in ophthalmic preparations; ophthalmic pharmaceutical solutions for the treatment of dry eye; solutions for use with contact lenses; otorhinolaryngological preparations; vitamins and mineral preparations for ophthalmic use; contact lens cleaning preparations; vials and tubes sold filled with ophthalmic pharmaceutical preparations; drop dispensing devices sold filled with ophthalmic pharmaceutical preparations

IC 009. US 021 023 026 036 038. G & S: Contact lenses; computer hardware and downloadable software for use in medical office management; contact lens cases for use in the cleaning, soaking and storage of contact lenses

IC 010. US 026 039 044. G & S: Surgical drapes, namely, disposable ophthalmic eye drapes; surgical sponges; surgical apparatus and instruments for ophthalmic surgery, namely, phacoemulsifiers, vitreoretinal surgical devices and lasers; surgical sutures and suture needles for ophthalmic surgery; surgical kits comprising surgical sutures and suture needles for ophthalmic surgery; instruments for ophthalmic surgery, namely, drainage tubes, ophthalmic surgical sponges, probes, infusion sleeves, irrigation/aspiration cannulae, light shields, light emitting diode (LED) apparatus for lighting, incorporated into medical instruments, cannulae, forceps, scissors and medical trays for carrying, storage and sterilization of surgical instruments; ophthalmic surgical kits comprising drainage tubes, disposable eye drapes, ophthalmic surgical sponges, probes, infusion sleeves, irrigation/aspiration cannulae, light shields, light emitting diode (LED) apparatus for lighting, incorporated into medical instruments, cannulae, forceps, scissors and medical trays for carrying, storage and sterilization of surgical instruments; intraocular lenses; optometric instruments for the insertion of intraocular lenses; surgical instruments and apparatus for use in ophthalmic surgery; microscopes for surgical operations and structural parts therefore

Mark Drawing Code

Serial Number

Filing Date

Current Basis

Original Filing Basis

Published for Opposition

Owner

Attorney of Record

Priority Date

Prior Registrations

Description of Mark

Type of Mark

Register

Live/Dead Indicator

(5) WORDS, LETTERS, AND/OR NUMBERS IN STYLIZED FORM

88378223

April 9, 2019

44E

1B;44D

April 5, 2022

(APPLICANT) Alcon Inc. CORPORATION SWITZERLAND Rue Louis-d'Affry 6 Fribourg SWITZERLAND CH-1701

Nancy Sabarra

February 4, 2019

0581463;1055870;1740936

The color blue is claimed as a feature of the mark. The mark consists of the word "**ALCON**" in stylized letters and in the color blue.

TRADEMARK

PRINCIPAL

LIVE

TESS HOME

NEW USER

STRUCTURED

FREE FORM

BROWSE DICT

SEARCH OG

TOP

HELP

PREV LIST

CURR LIST

NEXT LIST

FIRST DOC

PREV DOC

NEXT DOC

LAST DOC

EXHIBIT J





Making History Together: A Night of Innovation

Inspiring stories on innovation and
science in the world of Ophthalmology

SATURDAY, APRIL 23, 2022

National Museum of American History

7:00 P.M. – 9:00 P.M.

This program is non-CME.

Join us for a showcase of speakers telling their story of how the new Clareon® IOL Family, Hydrus® Microstent, ARGOS® Biometer, and SMART Solutions have transformed their practice and the lives of their patients. Your evening will start with a series of 10-minute inspiring stories followed by one-on-one discussions and hands-on demonstrations on Alcon’s technologies. You do not want to miss this special event!

FOR MORE INFORMATION, REGISTER AT
bit.ly/alconinnovation



MC



Elizabeth Yeu, MD
Norfolk, VA

FACULTY



Rosa Braga-Mele, MD
Toronto, ON



John Hovanesian, MD
Laguna Hills, CA



Cathleen McCabe, MD
Bradenton, FL

Sponsored by



All faculty and moderators are paid consultants of Alcon.



Introducing the Clareon® Collection of IOLs

SATURDAY, APRIL 23, 2022

Walter E. Washington Convention Center, Salon GH1

Registration and Lunch: 11:30 A.M.

Program: 12:00 P.M. – 1:00 P.M.

This program is non-CME.

REGISTER TODAY!
Meetings.EyeWorld.org/Clareon



MODERATOR



John Berdahl, MD
Sioux Falls, SD

FACULTY



Ashley Brissette, MD
New York, NY



Anna Fakadej, MD
Southern Pines, NC

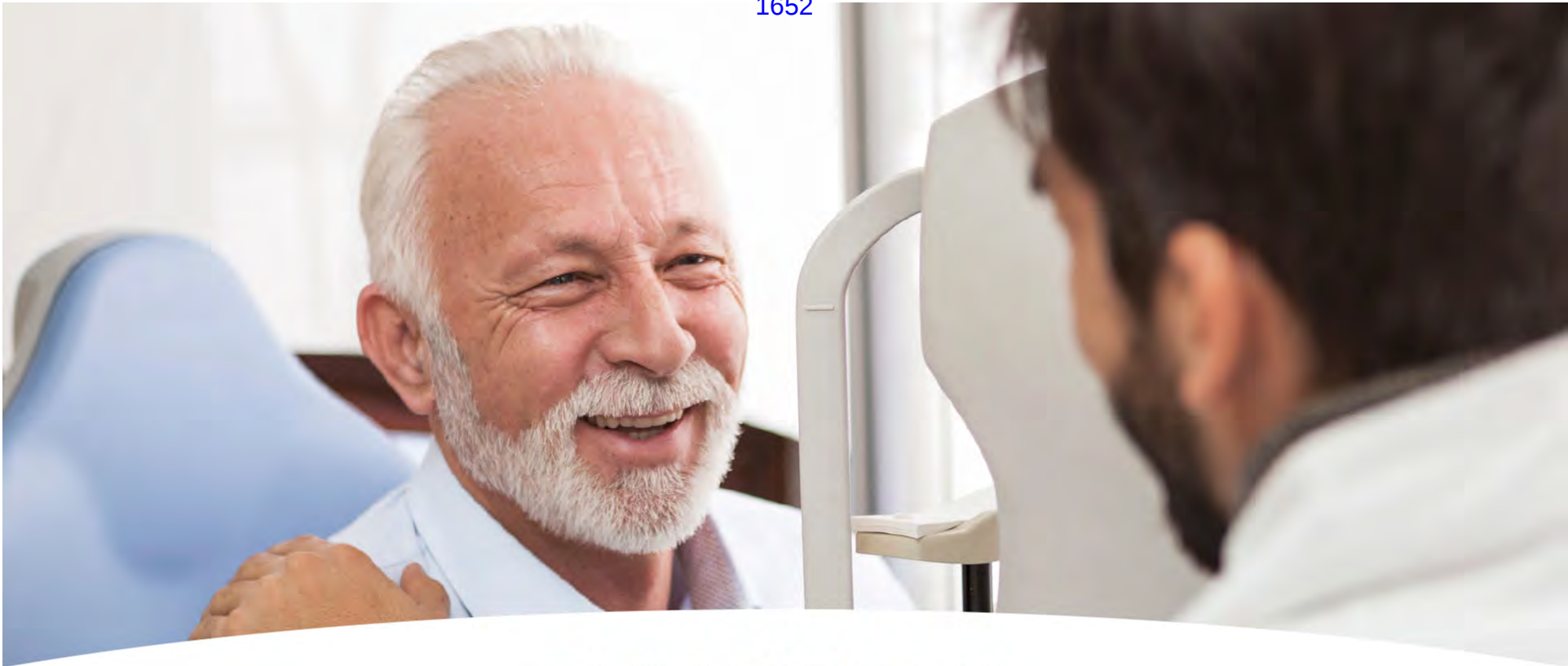


Bennett Walton, MD
Houston, TX

Sponsored by



All faculty and moderators are paid consultants of Alcon.



EYEWORLD
CORPORATE EDUCATION
Washington, D.C. 2022

Your MIGS Choice Matters:
A Hydrus® Microstent Discussion

SATURDAY, APRIL 23, 2022

Walter E. Washington Convention Center, Salon GH1

Registration: 5:00 P.M.

Program: 5:30 P.M. – 6:30 P.M.

This program is non-CME.

REGISTER TODAY!
Meetings.EyeWorld.org/Hydrus



MODERATOR



Leon Herndon, MD
Durham, NC

FACULTY



Nathan Radcliffe, MD
New York NY



Zarmeena Vendal, MD
Austin TX



William Wiley, MD
Cleveland OH

Sponsored by



All faculty and moderators are paid consultants of Alcon.



ALCON HELPS PEOPLE SEE BRILLIANTLY

Alcon Booth Experience

Discover Alcon’s latest advancements in Ophthalmology and Connectivity That Matters at **Booth #1411**:

- The Clareon® Collection of IOLs
- Diagnostics

- Surgical Glaucoma
- Visualization

- Refractive
- Dry Eye Devices

PRODUCT HIGHLIGHTS



LEARN MORE



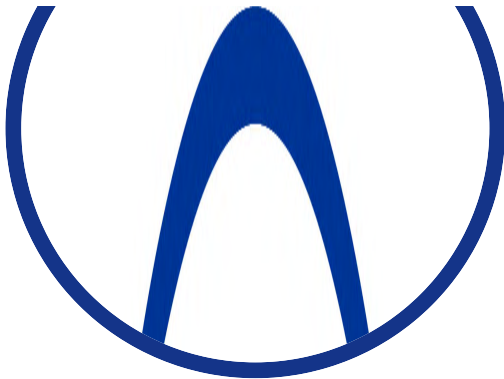
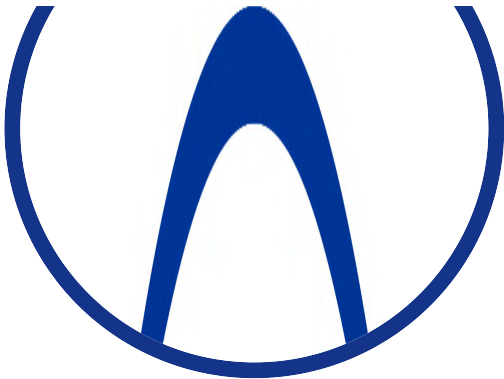
ARGOS[®]

with Image Guidance by **ALCON[®]**

LEARN MORE

<https://professional.myalcon.com/events/ascrs2022/>

7/10

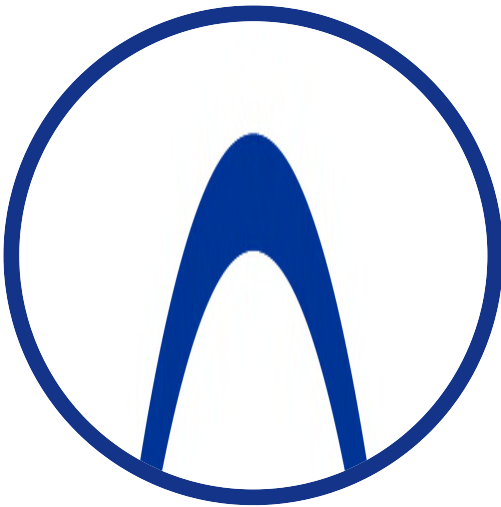


Alcon
Vision Suite

LEARN MORE



LEARN MORE



LEARN MORE

NEWS



LEARN MORE

CONNECT WITH US



FOLLOW



FOLLOW



FOLLOW

©2022 Alcon, Inc. 4/22 US-CLI-2200026

This communication is not affiliated with the official program of the ASCRS and ASOA 2022 Annual Meeting or any of its subsidiaries.



EXHIBIT K

TESS was last updated on Wed Jun 8 03:32:23 EDT 2022

TESS HOME

NEW USER

STRUCTURED

FREE FORM

BROWSE DICT

SEARCH OG

BOTTOM

HELP

PREV LIST

CURR LIST

NEXT LIST

FIRST DOC

PREV DOC

NEXT DOC

LAST DOC

Logout

Please logout when you are done to release system resources allocated for you.

Start

List At: OR

Jump

 to record: **Record 40 out of 988**

TSDR

ASSIGN Status

TTAB Status

(Use the "Back" button of the Internet Browser to return to TESS)

See Brilliantly

Word Mark

SEE BRILLIANTLY

Goods and Services

IC 003. US 001 004 006 050 051 052. G & S: Make-up remover; non-medicated eyelid cleansers

IC 005. US 006 018 044 046 051 052. G & S: Ophthalmic preparations; pharmaceutical preparations for the external treatment of hay fever; contrast media used intravenously as an aid to visualize abnormal conditions in the body and as a means of determining circulation time in the blood; contact lens wetting and soaking solutions; a mixture of water soluble polymers sold as an ingredient in ophthalmic preparations; decongestants; ophthalmic pharmaceutical solutions for the treatment of dry eye; solutions for use with contact lenses; otorhinolaryngological preparations; vitamins and mineral preparations for ophthalmic use; contact lens cleaning preparations; vials and tubes sold filled with ophthalmic pharmaceutical preparations; drop dispensing devices sold filled with ophthalmic pharmaceutical preparations

IC 009. US 021 023 026 036 038. G & S: Contact lenses; computer hardware and downloadable software for use in medical office management; contact lens cases for use in the cleaning, soaking and storage of contact lenses

IC 010. US 026 039 044. G & S: Surgical drapes, namely, disposable ophthalmic eye drapes; surgical sponges; surgical apparatus and instruments for ophthalmic surgery, namely, phacoemulsifiers, vitreoretinal surgical devices and lasers; surgical sutures and suture needles for ophthalmic surgery; surgical kits comprising surgical sutures and suture needles for ophthalmic surgery; instruments for ophthalmic surgery, namely, drainage tubes, ophthalmic surgical sponges, probes, infusion sleeves, irrigation/aspiration cannulae, light shields, light emitting diode (LED) apparatus for lighting, incorporated into medical instruments, cannulae, forceps, scissors and medical trays for carrying, storage and sterilization of surgical instruments; ophthalmic surgical kits comprising drainage tubes, disposable eye drapes, ophthalmic surgical sponges, probes, infusion sleeves, irrigation/aspiration cannulae, light shields, light emitting diode (LED) apparatus for lighting, incorporated into medical instruments, cannulae, forceps, scissors and medical trays for carrying, storage and sterilization of surgical instruments; intraocular lenses; optometric instruments for the insertion of intraocular lenses; surgical instruments and apparatus for use in ophthalmic surgery; microscopes for surgical operations and structural parts therefore

IC 035. US 100 101 102. G & S: Advertising; business management; business administration for others; providing office functions

IC 037. US 100 103 106. G & S: Building construction; repair of surgical equipment; installation of surgical equipment

IC 041. US 100 101 107. G & S: Educational services, namely, conducting classes, seminars, conferences, and workshops in the field of vision care; training services in the field of ophthalmology; organizing exhibitions for cultural purposes

Standard Characters Claimed	
Mark Drawing Code	(4) STANDARD CHARACTER MARK
Serial Number	88378309
Filing Date	April 9, 2019
Current Basis	1B
Original Filing Basis	1B;44D
Published for Opposition	December 10, 2019
Owner	(APPLICANT) Alcon Inc. CORPORATION SWITZERLAND Rue Louis-d'Affry 6 Fribourg SWITZERLAND CH-1701
Attorney of Record	Lisa Hart
Priority Date	February 4, 2019
Type of Mark	TRADEMARK. SERVICE MARK
Register	PRINCIPAL
Live/Dead Indicator	LIVE

TESS HOME

NEW USER

STRUCTURED

FREE FORM

BROWSE DICT

SEARCH OG

TOP

HELP

PREV LIST

CURR LIST

NEXT LIST

FIRST DOC

PREV DOC

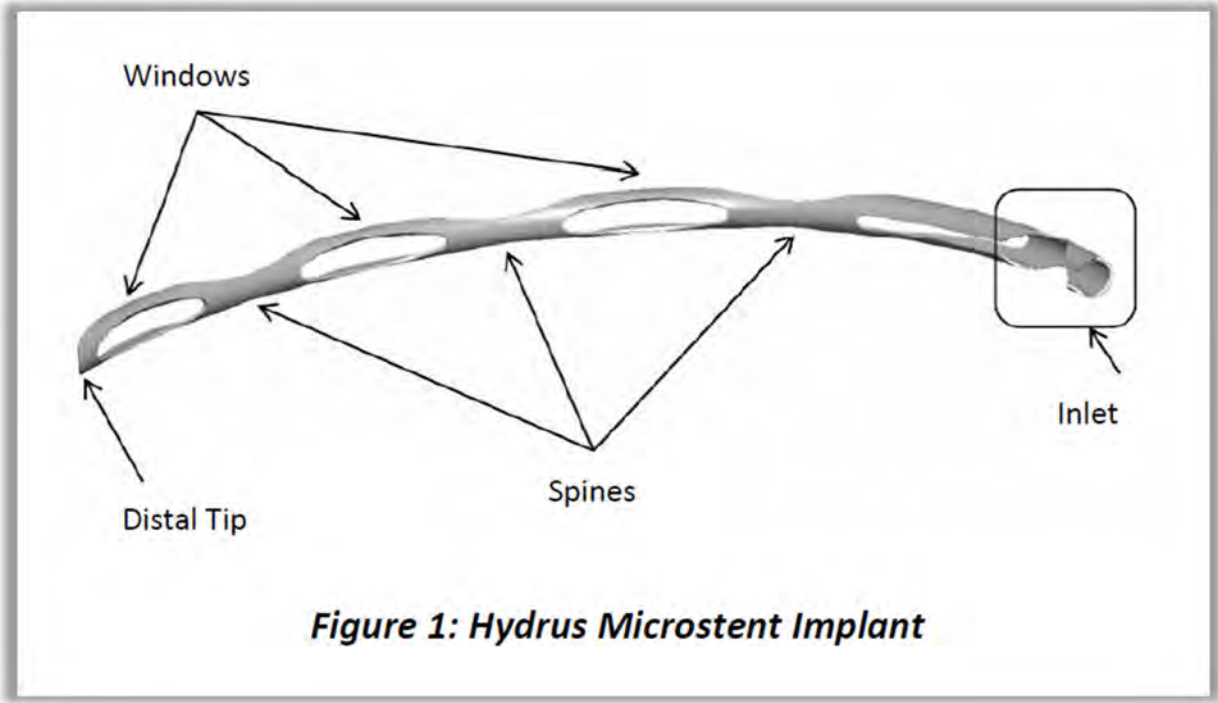
NEXT DOC

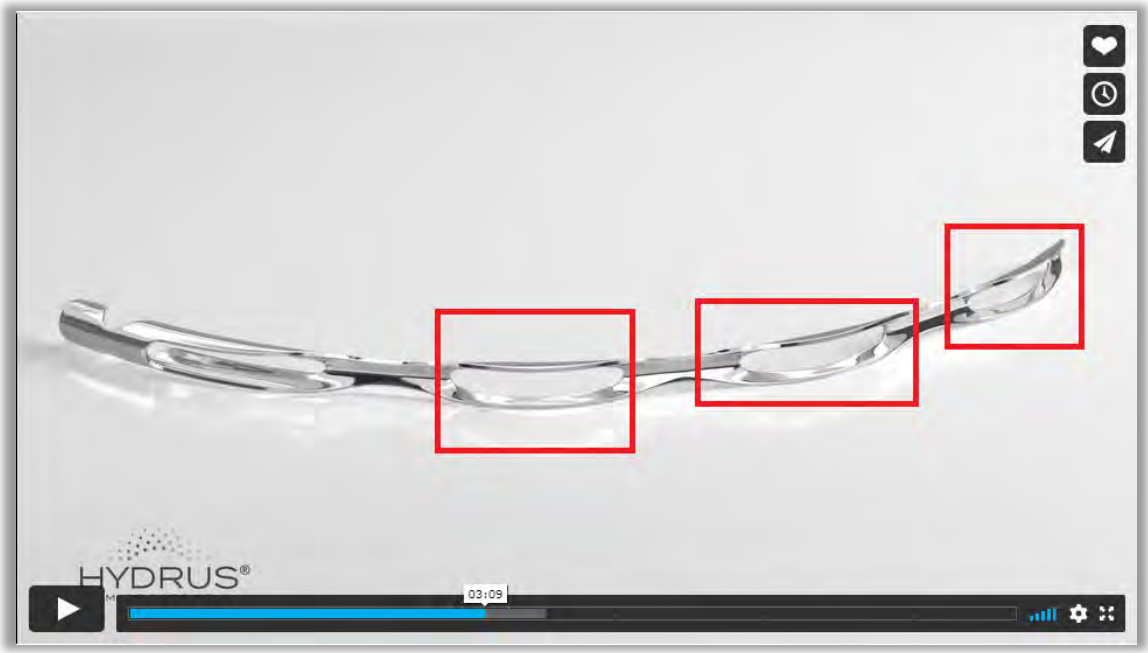
LAST DOC



EXHIBIT L


Exemplary Claim Chart of Hydrus® Microstent Against U.S. Patent No. 8,287,482 (“482 Patent”)

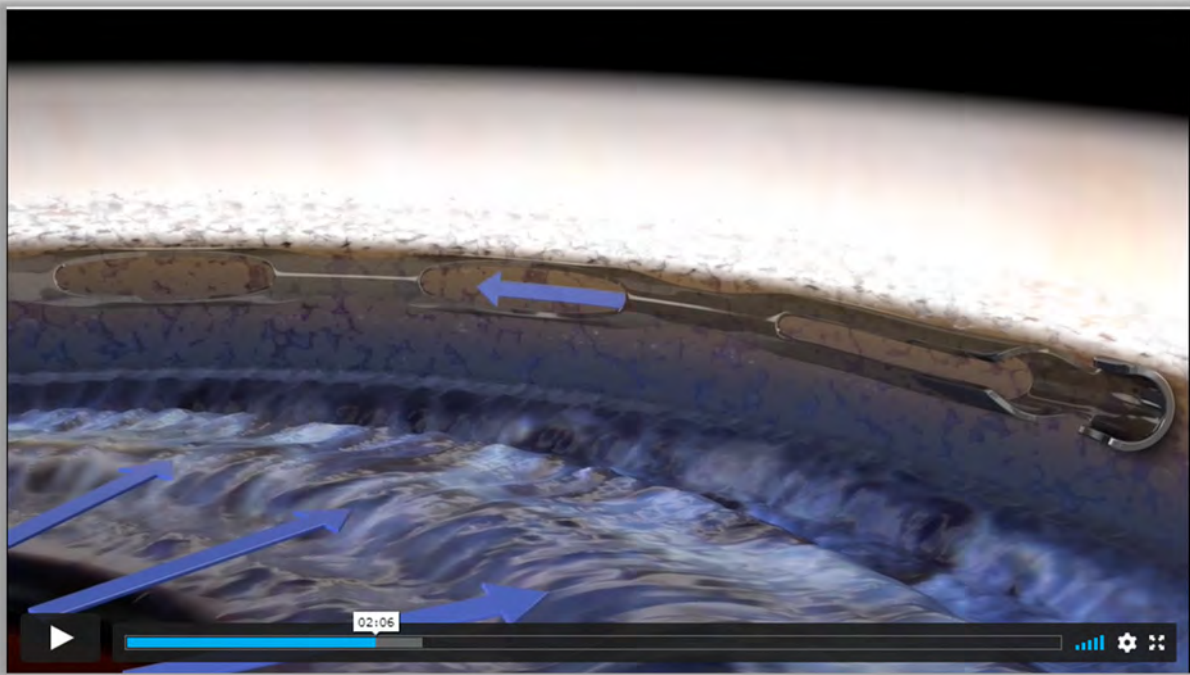
Claim [Limitation]	Evidence of Infringement
1[pre]: A device compromising:	<p>The Hydrus Microstent is a “device”:</p> <ul style="list-style-type: none"> • “The Hydrus microstent is an ab interno canal-based MIGS approach designed to optimize aqueous drainage. It is the first device to use a tri-modal mechanism of action to treat areas of resistance that inhibit aqueous flow in the eye.” (“IM-00 16-1-2 Rev B OUS Hydrus Microstent Animation (Full)”, https://vimeo.com/510821860 (hereinafter “Hydrus Animation”) at 1:56 – 2:14.) • “The Hydrus microstent is made of nitinol, a highly biocompatible and widely used material in biomedical applications. It is a tiny, flexible drainage device that is polished to a mirror-smooth finish and is typically neither seen nor felt by the patients.” (Hydrus Animation at 3:04-3:22.)
1[a]: a support having at least one fenestration that is longitudinally insertable into a lumen of Schlemm’s canal, the support having a cross-sectional dimension sufficient to at least partially prop open Schlemm’s canal upon insertion into the canal, and to thereby maintain patency of at least a portion of the canal so that fluid may traverse the canal without substantial interference from the support,	<p>The Hydrus Microstent is a “support.”</p> <ul style="list-style-type: none"> • “The microstent (Figure 1) is composed of nitinol, a metal alloy of nickel (Ni) and titanium (Ti). Nitinol has been used extensively in a variety of implantable devices for its proven properties of flexibility, strength and biocompatibility. As a shape memory alloy, nitinol has super-elastic properties making it suitable as a support structure in Schlemm's canal. The implant is laser cut from nitinol tubing to a proprietary design with alternating “spines” for structural support and “windows” to provide outflow pathways for aqueous humor. After laser cutting, the shape of the implant is heat-set to a curvature that matches the curvature of Schlemm’s canal and is electro-polished to create a smooth biocompatible surface. The microstent is approximately 8mm in overall length with major and minor axes of 292µm and 185µm, respectively. The length and curvature of the implant are designed to occupy approximately 90° or 3 clock hours of Schlemm’s canal. The implant is designed to have adequate structural thickness to support the tissue of the canal while providing maximum open flow areas through the canal, with the proximal portion of the implant exiting the canal through the trabecular meshwork to allow inflow of aqueous humor from the anterior chamber.” (IFU at 1.)

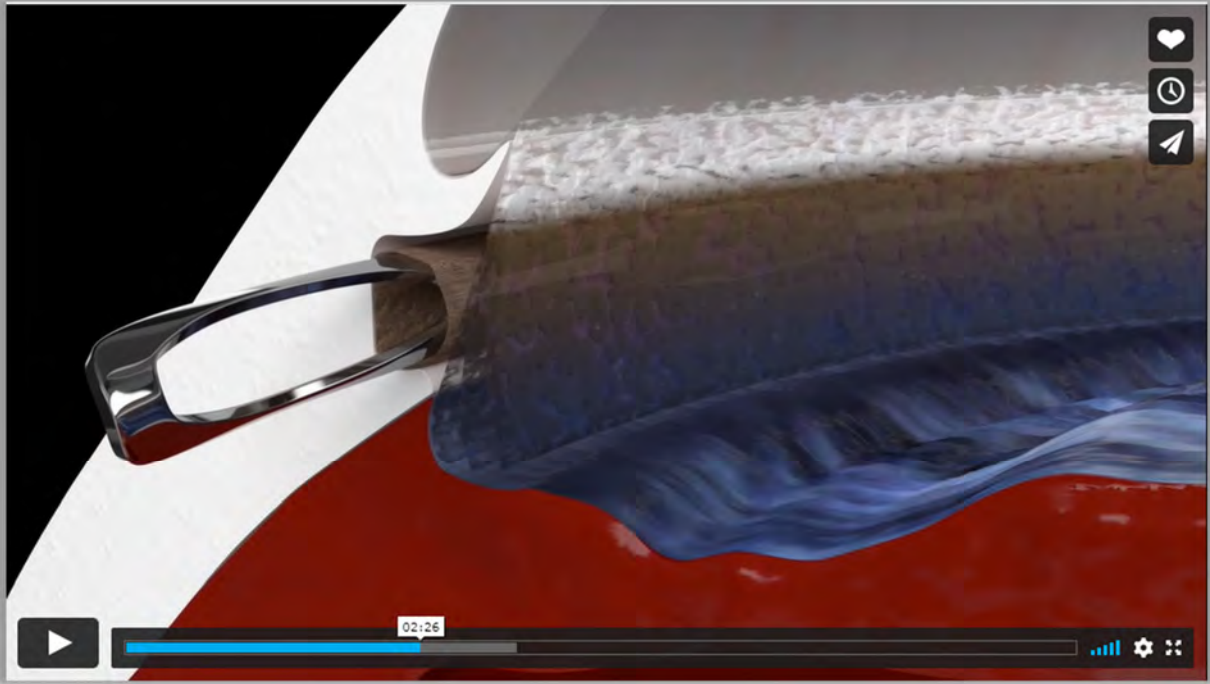
Claim [Limitation]	Evidence of Infringement
	<p data-bbox="569 237 1864 305">The Hydrus Microstent comprises a “at least one fenestration.” Specifically, the Hydrus Microstent comprises multiple “windows,” or fenestrations:</p> <div data-bbox="632 354 1843 1052"><p data-bbox="940 954 1549 998">Figure 1: Hydrus Microstent Implant</p></div> <p data-bbox="569 1109 1409 1144">(Hydrus Microstent Instructions for Use (hereinafter “IFU”) at 2.)</p>

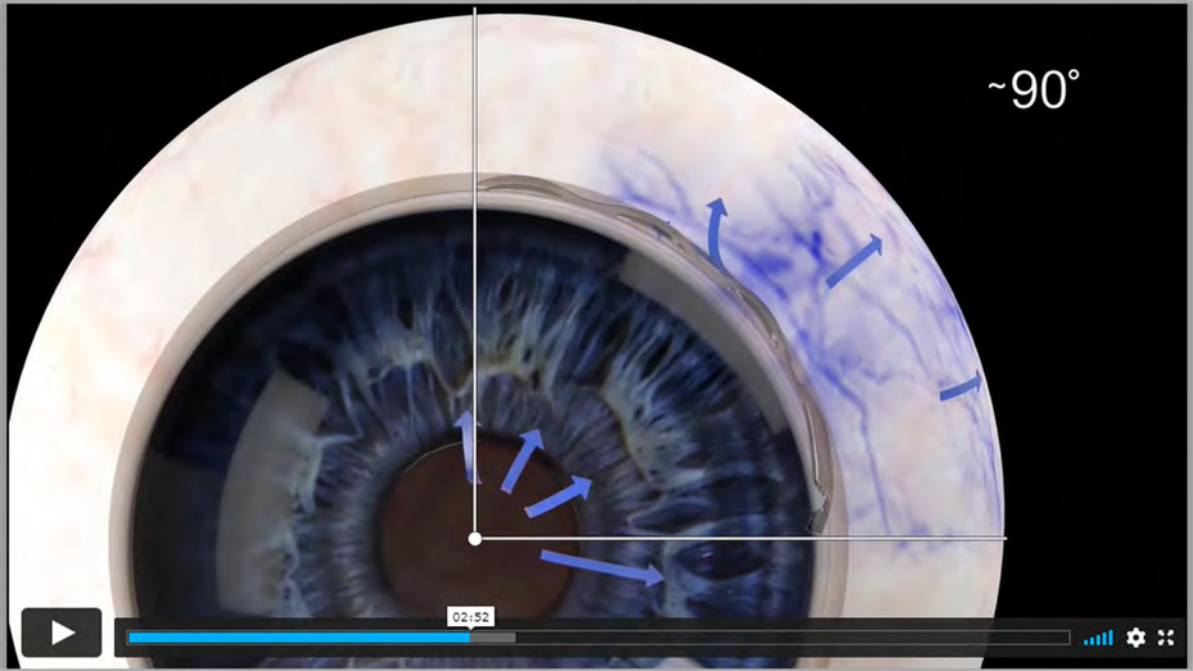
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="667 240 1808 889"></div> <p data-bbox="569 938 938 976">(Hydrus Animation at 3:09.)</p> <p data-bbox="569 1013 1724 1050">The Hydrus Microstent is “longitudinally insertable into a lumen of Schlemm’s canal”:</p>

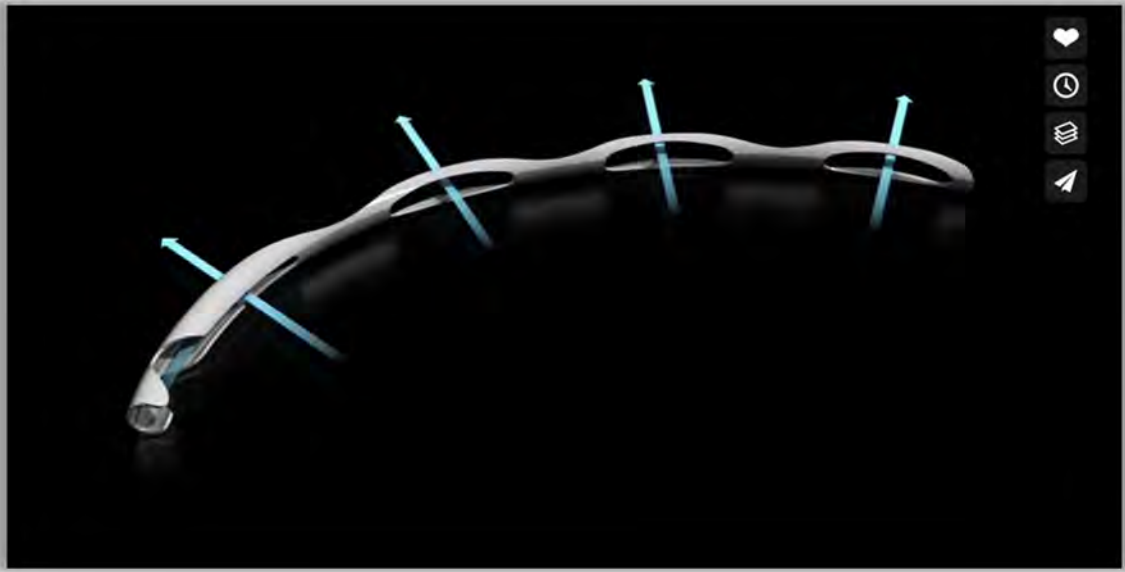
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="590 240 1724 488"> <p>Enhancing outflow</p> <p>Hydrus Microstent is placed in Schlemm's canal, a part of the drainage system of the eye. Fluid then flows along the canal (via the Hydrus Microstent) and into the eye's natural outflow channel to reduce eye pressure.*</p>  </div> <p>(https://www.ivantisinc.com/patients/understanding-hydrus/)</p> <div data-bbox="590 630 1724 943">  <p>Expanding the eye's natural fluid pathway</p> <p>Hydrus Microstent delicately expands the natural width of Schlemm's canal, allowing for enhanced flow through the eye's drainage system to help reduce eye pressure.</p> </div> <p>(https://www.ivantisinc.com/patients/understanding-hydrus/)</p> <ul style="list-style-type: none"> • “The microstent is implanted into the eye using a hand-held delivery system (Figure 2) that provides for delivery of the implant through a stainless steel cannula into the target site in the eye. The delivery system was designed to provide smooth tracking and controlled delivery of the microstent into Schlemm's canal. The delivery system is an ergonomic design for use in either the right or left hand, allowing for surgeon individual preference and hand position. To accommodate a wide range of hand positions, a rotatable sleeve at the distal end allows positioning and alignment of the cannula by the surgeon to direct the implant into Schlemm's canal. The tracking wheel on the delivery system serves as the control mechanism to advance the

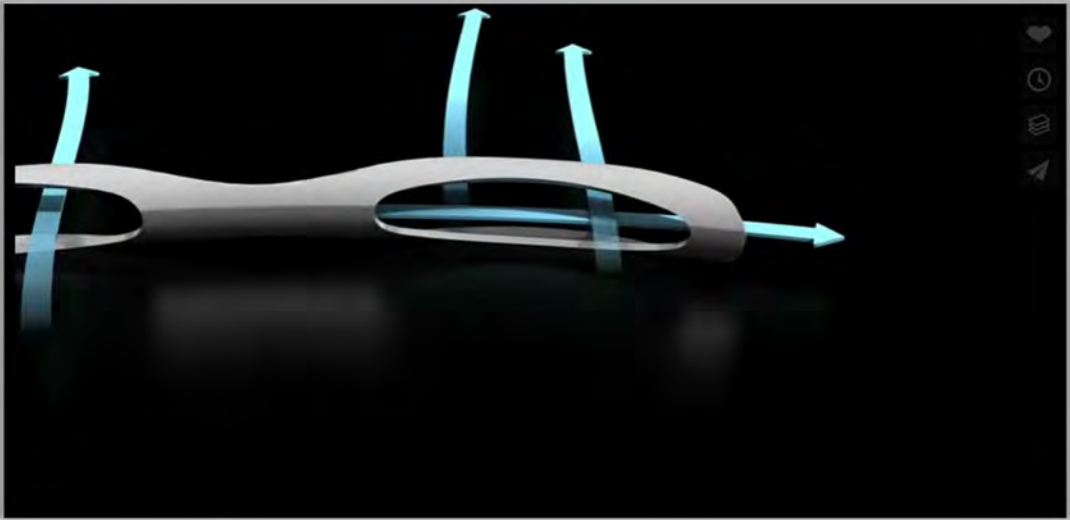
Claim [Limitation]	Evidence of Infringement
	<p>implant into the canal or retract the implant into the cannula. To deliver the microstent into Schlemm's canal, the cannula of the delivery system is inserted through a clear corneal incision (approximately 1.5 mm in length). The cannula tip is then advanced through the trabecular meshwork until it enters Schlemm's canal and the entry point into the meshwork is coincident with the end of the cannula bevel. The target tissue is visualized using a gonioscopic prism. After observing that the distal cannula tip is properly positioned through the trabecular meshwork into Schlemm's canal, the tracking wheel on the delivery system is used to advance and release the microstent." (IFU at 2-3.)</p> <div data-bbox="743 574 1776 1057" data-label="Image"> <p>Figure 5 shows the microstent positioned in Schlemm's canal with the proximal end (i.e., the inlet) protruding slightly into the anterior chamber for inflow of aqueous humor.</p>  <p><i>Figure 5: Microstent in Schlemm's Canal</i> (Proximal end at right accessing aqueous humor from the anterior chamber)</p> </div> <p>(IFU at 8.)</p> <p>The Hydrus Microstent has “a cross-sectional dimension sufficient to at least partially prop open Schlemm's canal upon insertion into the canal” and thereby “maintain[s] patency of at least a portion of the canal so that fluid may traverse the canal without substantial interference from the support.” Specifically, the Hydrus Microstent both scaffolds Schlemm's canal in order to dilate the</p>

Claim [Limitation]	Evidence of Infringement
	<p data-bbox="569 237 1871 302">canal, while also using an open design with multiple fenestrations to maintain flow of aqueous humor across the canal:</p> <div data-bbox="646 354 1829 1024"></div> <p data-bbox="569 1081 936 1114">(Hydrus Animation at 2:06.)</p>

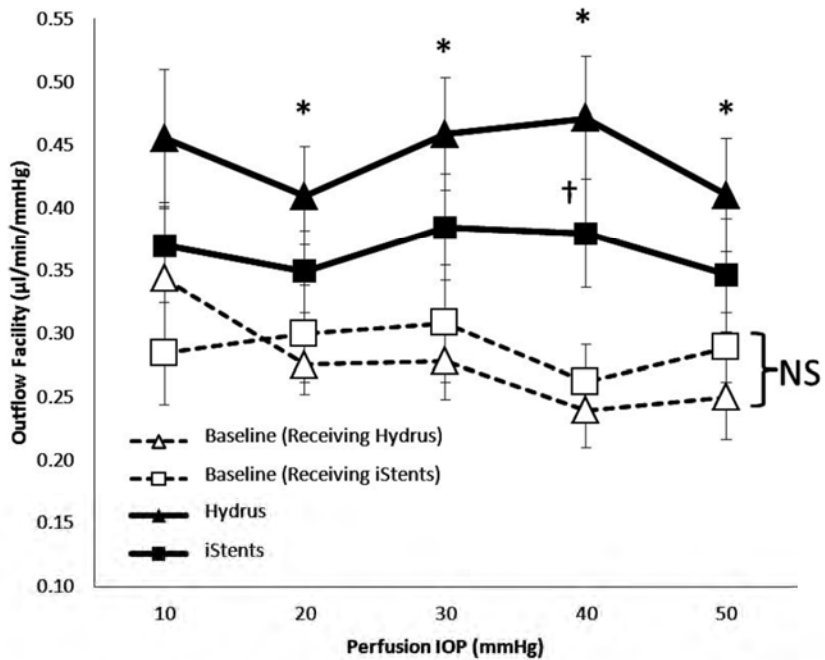
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="590 253 1793 932"></div> <p data-bbox="569 987 938 1027">(Hydrus Animation at 2:26.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="594 248 1780 914"></div> <p data-bbox="569 971 938 1008">(Hydrus Animation at 2:52.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="590 245 1709 813"></div> <p data-bbox="569 867 1808 938">("Hydrus Minimally Invasice [sic; "Invasive"] Glaucoma Surgery (MIGS)," (Hereinafter "MIGS Video") https://vimeo.com/169867478, at 1:10.)</p>

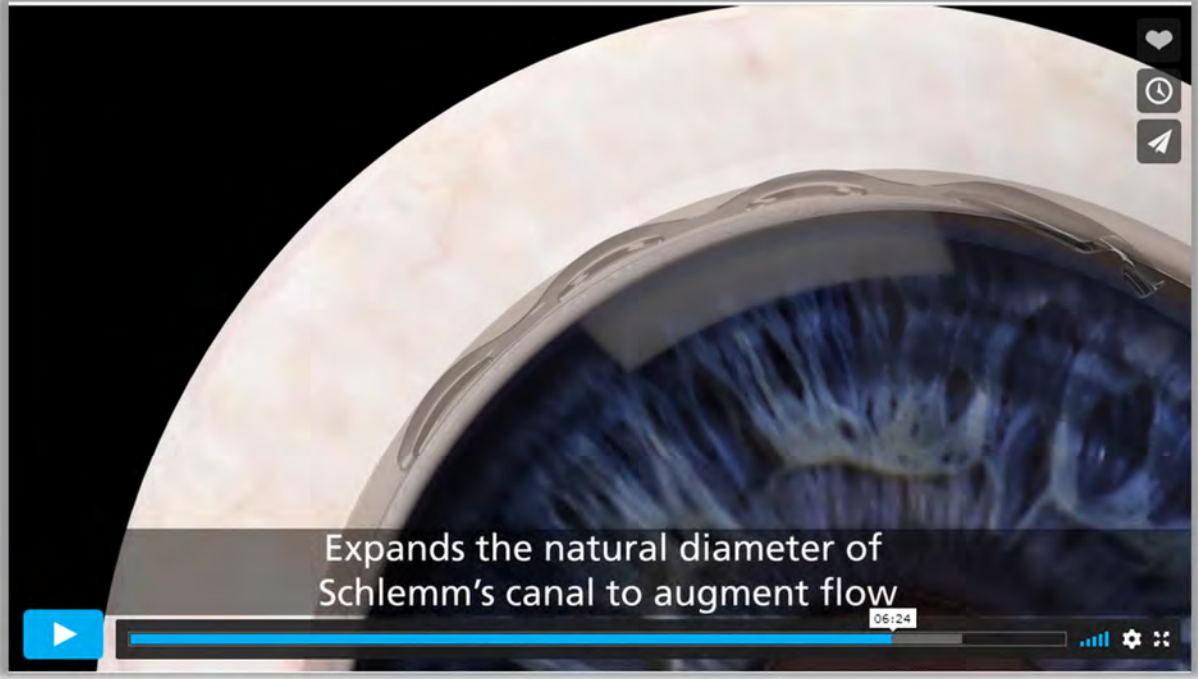
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="709 248 1772 764"></div> <p data-bbox="573 824 863 857">(MIGS Video at 1:50.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="730 245 1745 764" data-label="Image"> </div> <p data-bbox="573 824 863 854">(MIGS Video at 2:40.)</p> <ul style="list-style-type: none"> <li data-bbox="621 899 1898 1224">• “The Hydrus Microstent is an ab interno canal-based MIGS approach designed to optimize aqueous drainage. It is the first device to use a tri-modal mechanism of action to treat areas of resistance that inhibit aqueous flow in the eye. The Hydrus Microstent acts to bypass the obstructed trabecular meshwork by creating an optimal pathway for the aqueous to flow through Schlemm’s canal. Additionally, with its open scaffold design, the Microstent provides for a gentle dilation of a potentially narrowing or collapsing Schlemm’s canal. And because of its 8-millimeter length and approximate 90-degree span within Schlemm’s canal, the Hydrus allows for enhanced access and unobstructed flow into the numerous collector channels and network of aqueous outflow veins.” (Hydrus Animation at 1:57 – 2:50.) <li data-bbox="621 1269 1898 1372">• “The Hydrus Microstent is designed to reduce intraocular pressure by increasing aqueous flow through Schlemm’s canal, the eye’s natural outflow pathway. The Hydrus Microstent restores the flow of fluid in the eye using a trimodal mechanism of action. It creates a bypass through the

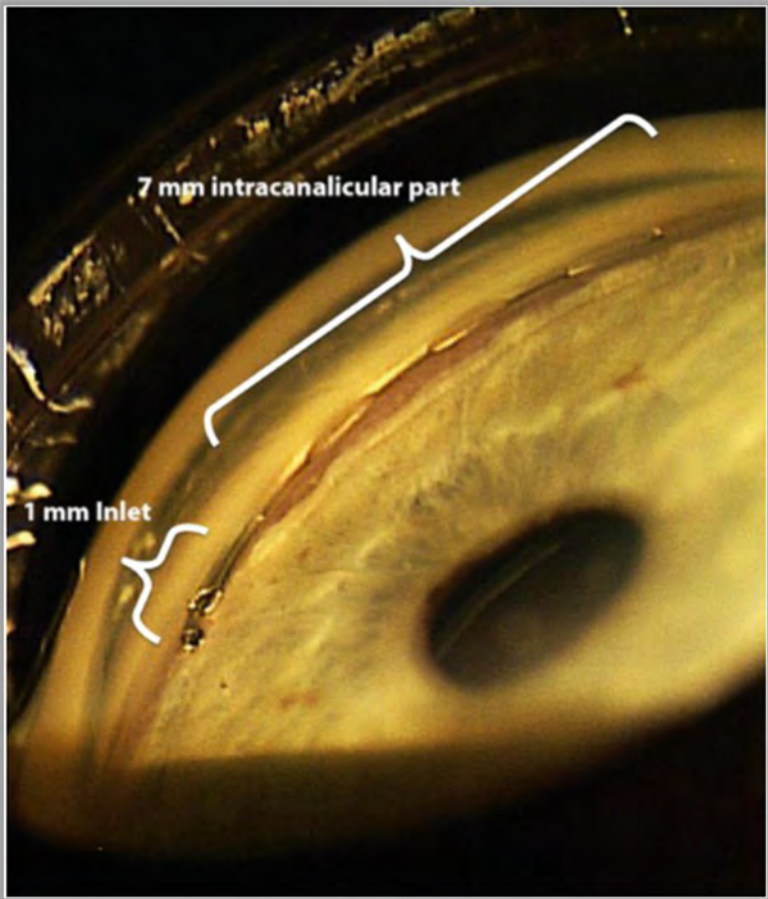
Claim [Limitation]	Evidence of Infringement
	<p>trabecular meshwork allowing flow from the anterior chamber into Schlemm's canal. The Hydrus Microstent scaffolds the canal, expanding the natural diameter to augment flow. It's length spans approximately 90 degrees of the canal, to provide access to the fluid collector channels in the eye." (Hydrus Animation at 5:52 - 6:35.)</p>  <p>FIGURE 3. Calculated outflow facilities (C) for anterior segments with implanted scaffold or two micro-bypasses. Bars represent SEM. *$P < 0.05$ for scaffold versus baseline 1. †$P < 0.05$ for two micro-bypasses versus baseline 2. Baseline measurements from contralateral eyes were not significantly different (NS).</p>

Claim [Limitation]	Evidence of Infringement																																																																							
	<p>(Cassandra L. Hays et al., “Improvement in Outflow Facility by Two Novel Microinvasive Glaucoma Surgery Implants,” 55:3 Investigative Ophthalmology & Visual Sci. 1893, 1896 (2014) (hereinafter “Hays”).)</p> <p>TABLE 2. Summary of Outflow Facilities Before and After Device Implantation</p> <table><tr><th rowspan="2">PP, mm Hg</th><th colspan="4">Scaffold</th><th colspan="4">2 Micro-Bypasses</th></tr><tr><th>Pre</th><th>Post</th><th>Change</th><th>P</th><th>Pre</th><th>Post</th><th>Change</th><th>P</th></tr><tr><td>10</td><td>0.34 ± 0.19</td><td>0.45 ± 0.19</td><td>0.07 ± 0.12</td><td>0.053</td><td>0.29 ± 0.14</td><td>0.37 ± 0.12</td><td>0.09 ± 0.16</td><td>0.09</td></tr><tr><td>20</td><td>0.28 ± 0.08</td><td>0.41 ± 0.13</td><td>0.13 ± 0.13</td><td>0.003</td><td>0.30 ± 0.13</td><td>0.35 ± 0.11</td><td>0.05 ± 0.15</td><td>0.27</td></tr><tr><td>30</td><td>0.28 ± 0.11</td><td>0.46 ± 0.15</td><td>0.18 ± 0.14</td><td>0.001</td><td>0.31 ± 0.16</td><td>0.39 ± 0.15</td><td>0.08 ± 0.18</td><td>0.17</td></tr><tr><td>40</td><td>0.24 ± 0.12</td><td>0.47 ± 0.17</td><td>0.23 ± 0.14</td><td><0.001</td><td>0.26 ± 0.10</td><td>0.38 ± 0.15</td><td>0.12 ± 0.13</td><td>0.01</td></tr><tr><td>50</td><td>0.25 ± 0.12</td><td>0.41 ± 0.16</td><td>0.16 ± 0.15</td><td>0.003</td><td>0.29 ± 0.09</td><td>0.35 ± 0.16</td><td>0.06 ± 0.11</td><td>0.09</td></tr><tr><td>Mean</td><td>0.28 ± 0.10</td><td>0.44 ± 0.13</td><td>0.16 ± 0.12</td><td>0.001</td><td>0.29 ± 0.09</td><td>0.37 ± 0.12</td><td>0.08 ± 0.12</td><td>0.046</td></tr></table> <p>Data are mean ± SD. Statistical significance between before and after device implantation was determined by paired <i>t</i>-tests. <i>n</i> = 12 pairs. PP, perfusion pressure.</p> <p>(Hays at 1897.)</p> <ul style="list-style-type: none">“Both implants effectively increased C [outflow facility] in human eyes ex vivo. The scaffold increased C by a greater percentage (73% vs. 34%) and at a greater range of perfusion pressures (20 to 50 mm Hg vs. 40 mm Hg) than the two micro-bypasses, suggesting that the 8-mm dilation of Schlemm’s canal by the scaffold may have additional benefits in lowering the outflow resistance. The Hydrus Microstent scaffold may be an effective therapy for increasing outflow facility and thus reducing the IOP in patients with glaucoma.” (Hays at 1893.)	PP, mm Hg	Scaffold				2 Micro-Bypasses				Pre	Post	Change	P	Pre	Post	Change	P	10	0.34 ± 0.19	0.45 ± 0.19	0.07 ± 0.12	0.053	0.29 ± 0.14	0.37 ± 0.12	0.09 ± 0.16	0.09	20	0.28 ± 0.08	0.41 ± 0.13	0.13 ± 0.13	0.003	0.30 ± 0.13	0.35 ± 0.11	0.05 ± 0.15	0.27	30	0.28 ± 0.11	0.46 ± 0.15	0.18 ± 0.14	0.001	0.31 ± 0.16	0.39 ± 0.15	0.08 ± 0.18	0.17	40	0.24 ± 0.12	0.47 ± 0.17	0.23 ± 0.14	<0.001	0.26 ± 0.10	0.38 ± 0.15	0.12 ± 0.13	0.01	50	0.25 ± 0.12	0.41 ± 0.16	0.16 ± 0.15	0.003	0.29 ± 0.09	0.35 ± 0.16	0.06 ± 0.11	0.09	Mean	0.28 ± 0.10	0.44 ± 0.13	0.16 ± 0.12	0.001	0.29 ± 0.09	0.37 ± 0.12	0.08 ± 0.12	0.046
PP, mm Hg	Scaffold				2 Micro-Bypasses																																																																			
	Pre	Post	Change	P	Pre	Post	Change	P																																																																
10	0.34 ± 0.19	0.45 ± 0.19	0.07 ± 0.12	0.053	0.29 ± 0.14	0.37 ± 0.12	0.09 ± 0.16	0.09																																																																
20	0.28 ± 0.08	0.41 ± 0.13	0.13 ± 0.13	0.003	0.30 ± 0.13	0.35 ± 0.11	0.05 ± 0.15	0.27																																																																
30	0.28 ± 0.11	0.46 ± 0.15	0.18 ± 0.14	0.001	0.31 ± 0.16	0.39 ± 0.15	0.08 ± 0.18	0.17																																																																
40	0.24 ± 0.12	0.47 ± 0.17	0.23 ± 0.14	<0.001	0.26 ± 0.10	0.38 ± 0.15	0.12 ± 0.13	0.01																																																																
50	0.25 ± 0.12	0.41 ± 0.16	0.16 ± 0.15	0.003	0.29 ± 0.09	0.35 ± 0.16	0.06 ± 0.11	0.09																																																																
Mean	0.28 ± 0.10	0.44 ± 0.13	0.16 ± 0.12	0.001	0.29 ± 0.09	0.37 ± 0.12	0.08 ± 0.12	0.046																																																																
1[b]: wherein when the support is disposed within a lumen of Schlemm’s canal, contact between the support and a wall of the canal is discontinuous along a perimeter of the	<p>The Hydrus Microstent is “disposed within a lumen of Schlemm’s canal.”</p> <ul style="list-style-type: none">“The microstent (Figure 1) is composed of nitinol, a metal alloy of nickel (Ni) and titanium (Ti). Nitinol has been used extensively in a variety of implantable devices for its proven properties of flexibility, strength and biocompatibility. As a shape memory alloy, nitinol has super-elastic properties making it suitable as a support structure in Schlemm’s canal. The implant is laser cut																																																																							

Claim [Limitation]	Evidence of Infringement
<p>lumen of the canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.</p>	<p>from nitinol tubing to a proprietary design with alternating “spines” for structural support and “windows” to provide outflow pathways for aqueous humor. After laser cutting, the shape of the implant is heat-set to a curvature that matches the curvature of Schlemm’s canal and is electro-polished to create a smooth biocompatible surface. The microstent is approximately 8mm in overall length with major and minor axes of 292µm and 185µm, respectively. The length and curvature of the implant are designed to occupy approximately 90° or 3 clock hours of Schlemm’s canal. The implant is designed to have adequate structural thickness to support the tissue of the canal while providing maximum open flow areas through the canal, with the proximal portion of the implant exiting the canal through the trabecular meshwork to allow inflow of aqueous humor from the anterior chamber.” (IFU at 1.)</p> <p><i>See also</i> claim 1[a], above.</p> <p>Furthermore, the contact between the support and a wall of the canal is “discontinuous along a perimeter of the lumen of the canal.” Specifically, as seen in the below screenshots, the Hydrus Microstent makes only periodic or discontinuous contact with the outer wall of the Schlemm’s canal in which it disposed:</p>

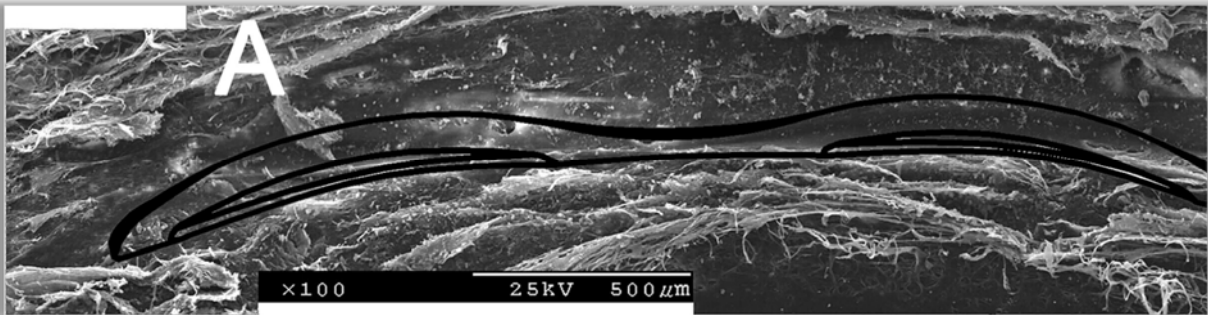
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="646 253 1837 927"><p>Expands the natural diameter of Schlemm's canal to augment flow</p></div> <p data-bbox="569 980 936 1019">(Hydrus Animation at 6:24.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="682 245 1791 722" data-label="Image"> <p>Figure 4: Preferred Position of Incisions and Target Placement of the Microstent</p> </div> <p data-bbox="569 781 709 813">(IFU at 6.)</p> <p data-bbox="569 854 1906 997">The Hydrus Microstent “contacts less than 30% of C,” wherein C is the surface area of a “cylindrical section of the lumen of the canal” in which the support is disposed. Approximately 7mm of the Hydrus Microstent is disposed within Schlemm’s canal once implanted, while an approximately 1mm inlet portion of the Microstent protrudes into Schlemm’s canal:</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="856 250 1619 1143"></div> <p data-bbox="569 1203 1908 1273">The 7mm portion of the Hydrus Microstent disposed within Schlemm's canal is comprised of a three "window regions," three "spine regions," and one "inlet spine region." According to the below figures,</p>

Claim [Limitation]	Evidence of Infringement																																																																																																																																							
	each window region spans 1.1 mm, each spine region spans 0.9 mm, and the inlet spine region spans 1.1 mm, for a total length of 7.1 mm:																																																																																																																																							
	<table><tr><th colspan="4">TABLE 1. Geometric Parameters of Implants</th></tr><tr><th>Parameters</th><th>Description</th><th>Value</th><th>Source</th></tr><tr><td colspan="4">8-mm scaffold</td></tr><tr><td>A_w</td><td>Area of window region</td><td>$17553 \mu\text{m}^2$</td><td>Ivantis</td></tr><tr><td>A_s</td><td>Area of spine region</td><td>$22955 \mu\text{m}^2$</td><td>Ivantis</td></tr><tr><td>A_{in}</td><td>Area of inlet spine region</td><td>$29841 \mu\text{m}^2$</td><td>Ivantis</td></tr><tr><td>h_w</td><td>Height of window region</td><td>$76.3 \mu\text{m}$</td><td>A_w/w_d</td></tr><tr><td>h_s</td><td>Height of spine region</td><td>$99.8 \mu\text{m}$</td><td>A_s/w_d</td></tr><tr><td>h_{in}</td><td>Height of inlet spine region</td><td>$129.7 \mu\text{m}$</td><td>A_{in}/w_d</td></tr><tr><td>L_w</td><td>Length of window region</td><td>1.1 mm</td><td>Ivantis</td></tr><tr><td>N_w</td><td>No. windows</td><td>3</td><td>Ivantis</td></tr><tr><td>w_d</td><td>Width of device</td><td>$230 \mu\text{m}$</td><td>Assumption</td></tr><tr><td>L_{in}</td><td>Length of inlet spine region</td><td>1.1 mm</td><td>Ivantis</td></tr><tr><td>L_{dev}</td><td>Length of device</td><td>7.2 mm</td><td>Ivantis</td></tr><tr><td>L_s</td><td>Length of spine region</td><td>0.9 mm</td><td>Ivantis</td></tr><tr><td colspan="4">15-mm scaffold</td></tr><tr><td>A_w</td><td>Area in window region</td><td>$20994 \mu\text{m}^2$</td><td>Ivantis</td></tr><tr><td>A_s</td><td>Area in device region</td><td>$32092 \mu\text{m}^2$</td><td>Ivantis</td></tr><tr><td>A_{in}</td><td>Area of inlet spine region</td><td>$29841 \mu\text{m}^2$</td><td>Ivantis</td></tr><tr><td>h_w</td><td>Height of window region</td><td>$91.3 \mu\text{m}$</td><td>A_w/w_d</td></tr><tr><td>h_s</td><td>Height of spine region</td><td>$139.5 \mu\text{m}$</td><td>A_s/w_d</td></tr><tr><td>h_{in}</td><td>Height of inlet spine region</td><td>$129.7 \mu\text{m}$</td><td>A_{in}/w_d</td></tr><tr><td>L_w</td><td>Length of window region</td><td>1 mm</td><td>Ivantis</td></tr><tr><td>N_w</td><td>No. windows</td><td>5</td><td>Ivantis</td></tr><tr><td>w_d</td><td>Width of device</td><td>$230 \mu\text{m}$</td><td>Assumption</td></tr><tr><td>L_{in}</td><td>Length of inlet spine region</td><td>1.1 mm</td><td>Ivantis</td></tr><tr><td>L_{dev}</td><td>Length of device</td><td>15 mm</td><td>Ivantis</td></tr><tr><td>L_s</td><td>Length of spine region</td><td>1.5 mm</td><td>Ivantis</td></tr><tr><td colspan="4">Trabecular microbypass</td></tr><tr><td>A_s</td><td>Area of device</td><td>$5652 \mu\text{m}^2$</td><td>$\pi 60^2/2$; cross-section is a half-circle with diameter of $120 \mu\text{m}$¹⁹</td></tr><tr><td>h_s</td><td>Height of device</td><td>$25.0 \mu\text{m}$</td><td>A_s/w_d</td></tr><tr><td>w_d</td><td>Width of device</td><td>$230 \mu\text{m}$</td><td>Assumption</td></tr><tr><td>L_{dev}</td><td>Length of device</td><td>1.0 mm</td><td>Samuelson et al¹⁹</td></tr></table>				TABLE 1. Geometric Parameters of Implants				Parameters	Description	Value	Source	8-mm scaffold				A_w	Area of window region	$17553 \mu\text{m}^2$	Ivantis	A_s	Area of spine region	$22955 \mu\text{m}^2$	Ivantis	A_{in}	Area of inlet spine region	$29841 \mu\text{m}^2$	Ivantis	h_w	Height of window region	$76.3 \mu\text{m}$	A_w/w_d	h_s	Height of spine region	$99.8 \mu\text{m}$	A_s/w_d	h_{in}	Height of inlet spine region	$129.7 \mu\text{m}$	A_{in}/w_d	L_w	Length of window region	1.1 mm	Ivantis	N_w	No. windows	3	Ivantis	w_d	Width of device	$230 \mu\text{m}$	Assumption	L_{in}	Length of inlet spine region	1.1 mm	Ivantis	L_{dev}	Length of device	7.2 mm	Ivantis	L_s	Length of spine region	0.9 mm	Ivantis	15-mm scaffold				A_w	Area in window region	$20994 \mu\text{m}^2$	Ivantis	A_s	Area in device region	$32092 \mu\text{m}^2$	Ivantis	A_{in}	Area of inlet spine region	$29841 \mu\text{m}^2$	Ivantis	h_w	Height of window region	$91.3 \mu\text{m}$	A_w/w_d	h_s	Height of spine region	$139.5 \mu\text{m}$	A_s/w_d	h_{in}	Height of inlet spine region	$129.7 \mu\text{m}$	A_{in}/w_d	L_w	Length of window region	1 mm	Ivantis	N_w	No. windows	5	Ivantis	w_d	Width of device	$230 \mu\text{m}$	Assumption	L_{in}	Length of inlet spine region	1.1 mm	Ivantis	L_{dev}	Length of device	15 mm	Ivantis	L_s	Length of spine region	1.5 mm	Ivantis	Trabecular microbypass				A_s	Area of device	$5652 \mu\text{m}^2$	$\pi 60^2/2$; cross-section is a half-circle with diameter of $120 \mu\text{m}$ ¹⁹	h_s	Height of device	$25.0 \mu\text{m}$	A_s/w_d	w_d	Width of device	$230 \mu\text{m}$	Assumption	L_{dev}	Length of device	1.0 mm	Samuelson et al ¹⁹
TABLE 1. Geometric Parameters of Implants																																																																																																																																								
Parameters	Description	Value	Source																																																																																																																																					
8-mm scaffold																																																																																																																																								
A_w	Area of window region	$17553 \mu\text{m}^2$	Ivantis																																																																																																																																					
A_s	Area of spine region	$22955 \mu\text{m}^2$	Ivantis																																																																																																																																					
A_{in}	Area of inlet spine region	$29841 \mu\text{m}^2$	Ivantis																																																																																																																																					
h_w	Height of window region	$76.3 \mu\text{m}$	A_w/w_d																																																																																																																																					
h_s	Height of spine region	$99.8 \mu\text{m}$	A_s/w_d																																																																																																																																					
h_{in}	Height of inlet spine region	$129.7 \mu\text{m}$	A_{in}/w_d																																																																																																																																					
L_w	Length of window region	1.1 mm	Ivantis																																																																																																																																					
N_w	No. windows	3	Ivantis																																																																																																																																					
w_d	Width of device	$230 \mu\text{m}$	Assumption																																																																																																																																					
L_{in}	Length of inlet spine region	1.1 mm	Ivantis																																																																																																																																					
L_{dev}	Length of device	7.2 mm	Ivantis																																																																																																																																					
L_s	Length of spine region	0.9 mm	Ivantis																																																																																																																																					
15-mm scaffold																																																																																																																																								
A_w	Area in window region	$20994 \mu\text{m}^2$	Ivantis																																																																																																																																					
A_s	Area in device region	$32092 \mu\text{m}^2$	Ivantis																																																																																																																																					
A_{in}	Area of inlet spine region	$29841 \mu\text{m}^2$	Ivantis																																																																																																																																					
h_w	Height of window region	$91.3 \mu\text{m}$	A_w/w_d																																																																																																																																					
h_s	Height of spine region	$139.5 \mu\text{m}$	A_s/w_d																																																																																																																																					
h_{in}	Height of inlet spine region	$129.7 \mu\text{m}$	A_{in}/w_d																																																																																																																																					
L_w	Length of window region	1 mm	Ivantis																																																																																																																																					
N_w	No. windows	5	Ivantis																																																																																																																																					
w_d	Width of device	$230 \mu\text{m}$	Assumption																																																																																																																																					
L_{in}	Length of inlet spine region	1.1 mm	Ivantis																																																																																																																																					
L_{dev}	Length of device	15 mm	Ivantis																																																																																																																																					
L_s	Length of spine region	1.5 mm	Ivantis																																																																																																																																					
Trabecular microbypass																																																																																																																																								
A_s	Area of device	$5652 \mu\text{m}^2$	$\pi 60^2/2$; cross-section is a half-circle with diameter of $120 \mu\text{m}$ ¹⁹																																																																																																																																					
h_s	Height of device	$25.0 \mu\text{m}$	A_s/w_d																																																																																																																																					
w_d	Width of device	$230 \mu\text{m}$	Assumption																																																																																																																																					
L_{dev}	Length of device	1.0 mm	Samuelson et al ¹⁹																																																																																																																																					

Claim [Limitation]	Evidence of Infringement
	<p>(Fan Yuan, <i>et al.</i>, “Mathematical Modeling of Outflow Facility Increase with Trabecular Meshwork Bypass and Schlemm Canal Dilation,” 25 J. Glaucoma 355, 358 (2016))</p> <p>The total surface area of the Hydrus Microstent is 0.057 cm², or 5,700,00 μm² (Srinidhi Nagaraja and Alan R. Pelton, <i>Corrosion resistance of a Nitinol ocular microstent: Implications on biocompatibility</i>, J. Biomed Mater Res. 108B:2681-2690 (2020).)</p> <p>Using dimensions and surface area figures reported by Yuan, et al., and Nagaraja and Pelton, the surface area of the Hydrus Microstent that potentially might contact the interior wall of Schlemm’s canal can be calculated as the total surface area (5,700,000 μm²), minus the area of the inlet portion that resides in the anterior chamber (60% of the lateral area of a cylinder with a radius of 146 μm and length of 900 μm), minus the outside edge area (60 μm * 16750μm), minus window edge area (60 μm * 3 * circumference of an oval of length 1100 μm and height of 200 μm), minus the inlet spine second edge area (60 μm * 2200 μm), divided in half. The resulting surface area that could potentially contact Schlemm’s canal is approximately 1,793,871 μm² which is less than 30% of a 7.1 mm cylinder with a radius of 146 μm.</p> <p>Furthermore, because the Hydrus Microstent makes only discontinuous contact with Schlemm’s canal, the potential area of contact is substantially less than 1,793,871 μm².</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="592 245 1793 558"></div> <p data-bbox="571 581 1890 651">(Johnstone et al., “Effects of a Schlemm Canal Scaffold on Collector Channel Ostia in Human Anterior Segments,” 119 Experimental Eye Research 70 (2014).)</p> <p data-bbox="571 691 1860 761">Specifically, while the window regions of the Hydrus scaffold and dilate the canal, the areas between the window regions have limited contact with the canal wall.</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="766 248 1703 948" data-label="Image"> <p>A histological section of a Hydrus microstent implant. The implant is a curved, pinkish structure with a central lumen, positioned within a larger, irregularly shaped canal (Schlemm's canal). The surrounding tissue is stained pink. A scale bar in the bottom right corner indicates 200 μm. The letter 'a' is in the top left corner of the image.</p> </div> <p>(Saba Samet, et al., <i>Hydrus microstent implantation for surgical management of glaucoma: a review of design, efficacy and safety</i>, Eye and Vision, Vol. 6, No. 32 (2019).)</p> <p>The Hydrus Microstent IFU and promotional materials additionally confirm that the Hydrus Microstent is designed so as to minimize surface area contact between the implant and the interior wall of Schlemm's canal, so as to maximize open flow of aqueous humor across and through the canal.</p> <ul style="list-style-type: none"> • “The microstent is approximately 8mm in overall length with major and minor axes of 292μm and 185μm, respectively. The length and curvature of the implant are designed to occupy approximately 90° or 3 clock hours of Schlemm's canal. The implant is designed to have

Claim [Limitation]	Evidence of Infringement
	<p>adequate structural thickness to support the tissue of the canal while providing maximum open flow areas through the canal, with the proximal portion of the implant exiting the canal through the trabecular meshwork to allow inflow of aqueous humor from the anterior chamber.” (IFU at 1.)</p> <ul style="list-style-type: none"> • “The Hydrus Microstent is an ab interno canal-based MIGS approach designed to optimize aqueous drainage. It is the first device to use a tri-modal mechanism of action to treat areas of resistance that inhibit aqueous flow in the eye. The Hydrus Microstent acts to bypass the obstructed trabecular meshwork by creating an optimal pathway for the aqueous to flow through Schlemm’s canal. Additionally, with its open scaffold design, the Microstent provides for a gentle dilation of a potentially narrowing or collapsing Schlemm’s canal. And because of its 8-millimeter length and approximate 90-degree span within Schlemm’s canal, the Hydrus allows for enhanced access and unobstructed flow into the numerous collector channels and network of aqueous outflow veins.” (Hydrus Animation at 1:57 – 2:50.)

Claim [Limitation]	Evidence of Infringement
63[pre]: A method for reducing intraocular pressure in an eye, the method comprising:	<p>The Hydrus Microstent implantation procedure is a “method for reducing intraocular pressure”:</p> <ul style="list-style-type: none"> • “Ivantis, a company dedicated to the development of innovative solutions for glaucoma therapy brings you the Hydrus Microstent, a groundbreaking MIGS technology designed to relieve the high intraocular pressure of the eye that is common in patients with primary open angle glaucoma.” (Hydrus Animation at 1:35 – 1:55.) • “The Hydrus Microstent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG).” (IFU at 3.)
63[a]: inserting a support having at least one	See claim 1[a] above.

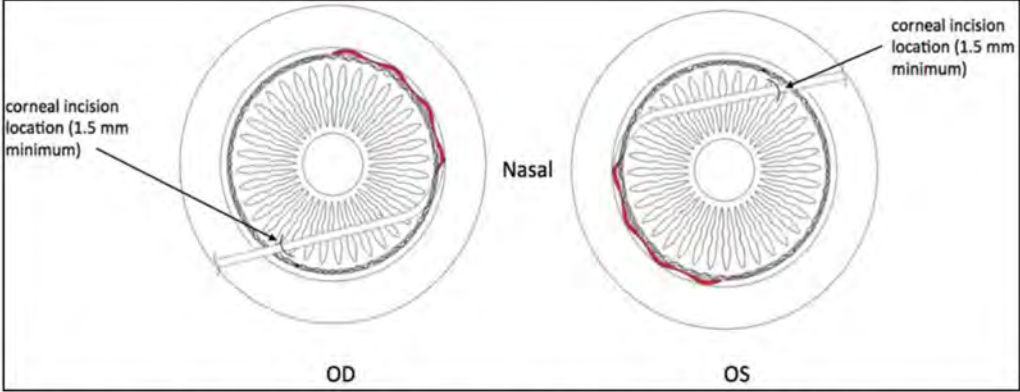
fenestration into a lumen of Schlemm's canal to at least partially prop open the canal and thereby maintain patency of at least a portion of the canal,	
63[b]: wherein when the support is disposed within the lumen of Schlemm's canal, the support allows fluid to traverse the canal without substantial interference from the support, and wherein contact between the support and a wall of the canal is discontinuous along a perimeter of the lumen of the canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.	<i>See claim 1[a], 1[b] above.</i>

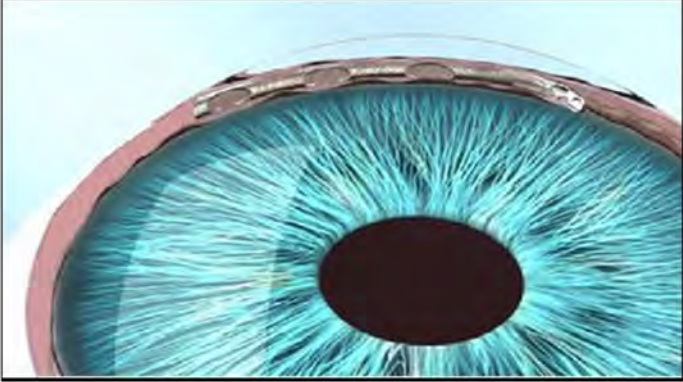
EXHIBIT M

Exemplary Claim Chart of Hydrus® Microstent Against U.S. Patent No. 9,370,443 (“443 Patent”)


Claim [Limitation]	Evidence of Infringement
<p>1[pre]: A device for reducing intraocular pressure in an eye having a Schlemm’s canal and a trabecular meshwork, comprising:</p>	<p>The Hydrus Microstent is a “device for reducing intraocular pressure in an eye having a Schlemm’s canal and a trabecular meshwork”:</p> <ul style="list-style-type: none"> • “Ivantis, a company dedicated to the development of innovative solutions for glaucoma therapy brings you the Hydrus Microstent, a groundbreaking MIGS technology designed to relieve the high intraocular pressure of the eye that is common in patients with primary open angle glaucoma.” (“IM-00 16-1-2 Rev B OUS Hydrus Microstent Animation (Full)”, https://vimeo.com/510821860 (hereinafter “Hydrus Animation”) at 1:35 – 1:55.) • “The Hydrus Microstent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG).” (Hydrus Microstent Instructions for Use (hereinafter “IFU”), at 3.) • “In a healthy functioning human eye, a structure in the posterior chamber just beneath the iris called the ciliary body secretes a clear, watery fluid called aqueous humor. This fluid flows in an unobstructed manner through the pupil and into the anterior chamber of the eye where it exists through the eye’s drainage system, consisting of a three-layered network of cells called the trabecular meshwork and an oval-shaped channel known as Schlemm’s canal. It is here where the aqueous is freely distributed into a series of collector channels and further into the episcleral venous system for outflow into the bloodstream. Over time, in primary open angle glaucoma, the trabecular meshwork may become obstructed, resulting in aqueous fluid accumulation and the inability to drain adequately through the natural drainage channel. This blockage to aqueous drainage causes the intraocular pressure or IOP in the anterior chamber of the eye to rise. This increase in IOP may negatively affect all the structures in the eye, but most importantly the optic nerve. Damage to the optic nerve may result in a decrease in peripheral vision that may eventually lead to blindness.” (Hydrus Animation at 0:00 – 1:35.)

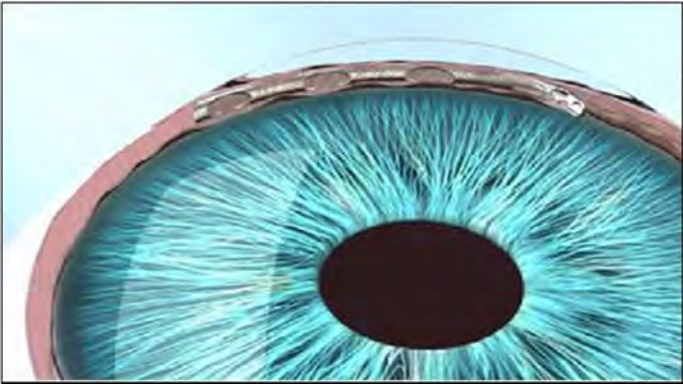
Claim [Limitation]	Evidence of Infringement
<p>1[a]: a support implantable circumferentially within Schlemm's canal and configured to maintain the patency of at least a portion thereof</p>	<p>The Hydrus Microstent is a “support.”</p> <ul style="list-style-type: none"> • “The microstent (Figure 1) is composed of nitinol, a metal alloy of nickel (Ni) and titanium (Ti). Nitinol has been used extensively in a variety of implantable devices for its proven properties of flexibility, strength and biocompatibility. As a shape memory alloy, nitinol has super-elastic properties making it suitable as a support structure in Schlemm's canal. The implant is laser cut from nitinol tubing to a proprietary design with alternating “spines” for structural support and “windows” to provide outflow pathways for aqueous humor. After laser cutting, the shape of the implant is heat-set to a curvature that matches the curvature of Schlemm's canal and is electro-polished to create a smooth biocompatible surface. The microstent is approximately 8mm in overall length with major and minor axes of 292µm and 185µm, respectively. The length and curvature of the implant are designed to occupy approximately 90° or 3 clock hours of Schlemm's canal. The implant is designed to have adequate structural thickness to support the tissue of the canal while providing maximum open flow areas through the canal, with the proximal portion of the implant exiting the canal through the trabecular meshwork to allow inflow of aqueous humor from the anterior chamber.” (IFU at 1.) <p>The Hydrus Microstent is “implantable circumferentially within Schlemm's canal.”</p>

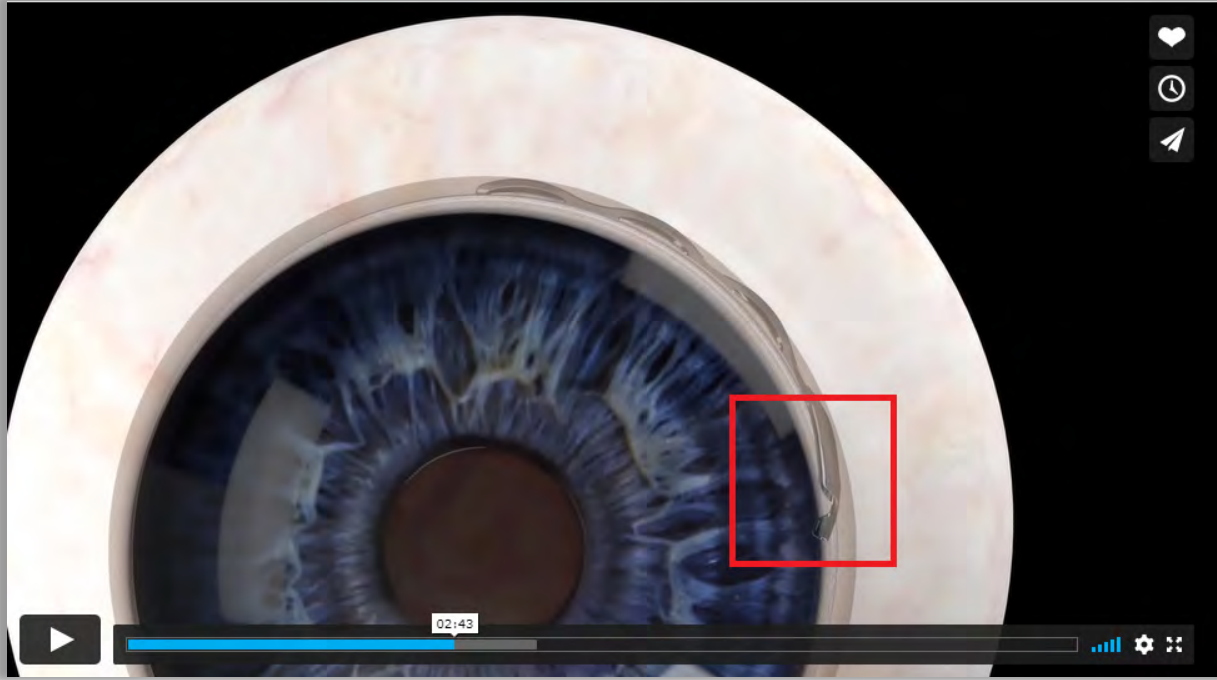
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="638 266 1745 743"><p data-bbox="730 699 1625 727"><i>Figure 4: Preferred Position of Incisions and Target Placement of the Microstent</i></p></div> <p data-bbox="516 800 653 833">(IFU at 6.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="583 264 1793 829" data-label="Image">  <p data-bbox="606 719 1776 800">Figure 5: Microstent in Schlemm's Canal (Proximal end at right accessing aqueous humor from the anterior chamber)</p> </div> <p data-bbox="516 886 653 919">(IFU at 8.)</p> <p data-bbox="516 963 1814 1027">The Hydrus Microstent is “configured to maintain the patency of at least a portion” of Schlemm’s canal:</p> <ul data-bbox="564 1073 1862 1321" style="list-style-type: none"> • “The Hydrus Microstent is an ab interno canal-based MIGS approach designed to optimize aqueous drainage. It is the first device to use a tri-modal mechanism of action to treat areas of resistance that inhibit aqueous flow in the eye. The Hydrus Microstent acts to bypass the obstructed trabecular meshwork by creating an optimal pathway for the aqueous to flow through Schlemm’s canal. Additionally, with its open scaffold design, the Microstent provides for a gentle dilation of a potentially narrowing or collapsing Schlemm’s canal. And because of its 8-millimeter length and approximate 90-degree span within Schlemm’s canal, the Hydrus allows

Claim [Limitation]	Evidence of Infringement
	<p>for enhanced access and unobstructed flow into the numerous collector channels and network of aqueous outflow veins.” (Hydrus Animation at 1:57 – 2:50.)</p> <ul style="list-style-type: none"> • “The Hydrus Microstent is designed to reduce intraocular pressure by increasing aqueous flow through Schlemm’s canal, the eye’s natural outflow pathway. The Hydrus Microstent restores the flow of fluid in the eye using a trimodal mechanism of action. It creates a bypass through the trabecular meshwork allowing flow from the anterior chamber into Schlemm’s canal. The Hydrus Microstent scaffolds the canal, expanding the natural diameter to augment flow. It’s length spans approximately 90 degrees of the canal, to provide access to the fluid collector channels in the eye.” (Hydrus Animation at 5:52 - 6:35.)
1[b]: wherein the support comprises an arcuate member	The Hydrus Microstent comprises an “ arcuate member. ”

Claim [Limitation]	Evidence of Infringement
	 <p>(Hydrus Animation at 6:44.)</p> <p><i>See also</i> claim 1[a], above.</p>
<p>1[c]: wherein at least a portion of the arcuate member has a radius of curvature smaller than the radius of curvature of</p>	<p>At least a portion of the Hydrus Microstent has a “radius smaller than the radius of the curvature of Schlemm’s canal.” Specifically, once implanted, the overall radius of the Hydrus Microstent is smaller than that of Schlemm’s canal, as evidenced by the fact that it protrudes at one end out of Schlemm’s canal and into the anterior chamber. Thus, at least a portion of the Hydrus Microstent is “configured to extend out of Schlemm’s canal and into the trabecular meshwork”:</p>

Claim [Limitation]	Evidence of Infringement
<p>Schlemm's canal so that at least a portion of the arcuate member is configured to extend out of Schlemm's canal and into the trabecular meshwork</p>	<div data-bbox="583 264 1797 833"><p>Figure 5: Microstent in Schlemm's Canal (Proximal end at right accessing aqueous humor from the anterior chamber)</p></div> <p>(IFU at 8.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="583 272 1793 948"></div> <p data-bbox="514 1008 1262 1045">(Hydrus Animation at 2:43 (red box added for emphasis).)</p>

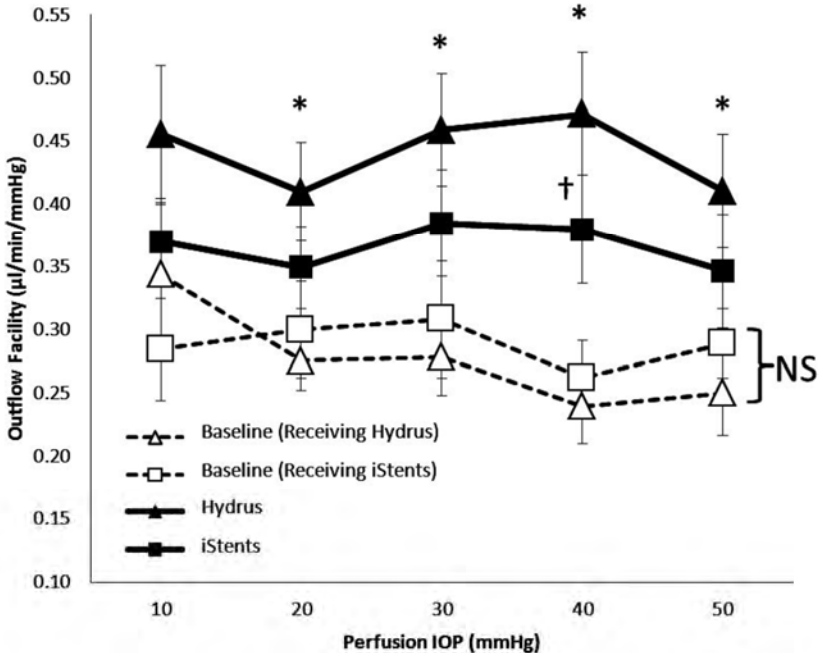
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="592 272 1785 945" data-label="Image"> </div> <p data-bbox="514 1003 882 1040">(Hydrus Animation at 5:32.)</p> <ul style="list-style-type: none"> <li data-bbox="562 1084 1801 1187"> <p>“Continue to advance the microstent until a physical stop is felt and the interlock releases the microstent. Verify that the inlet of the microstent is positioned in the anterior chamber.” (IFU at 7.)</p>
1[d]: and wherein the support does not substantially interfere	The Hydrus Microstent “ does not substantially interfere with transmural flow across Schlemm’s canal. ”:

Claim [Limitation]	Evidence of Infringement
with transmural flow across Schlemm's canal	<div data-bbox="537 272 1776 971"></div> <p data-bbox="516 1029 882 1065">(Hydrus Animation at 5:56.)</p>

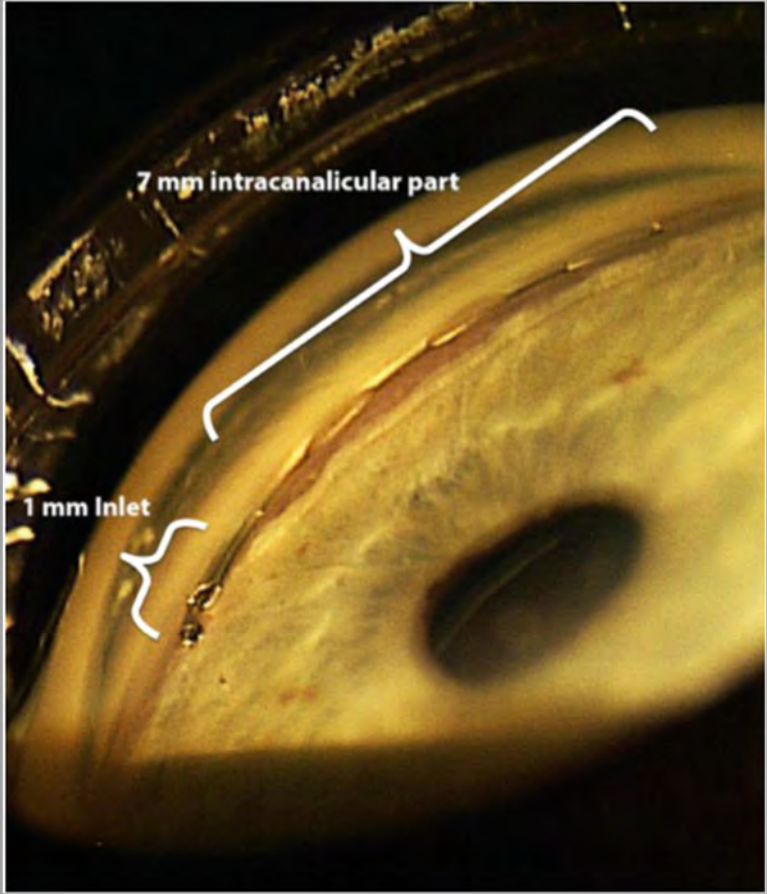
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="627 264 1745 833"></div> <p data-bbox="516 885 1755 956"> (“Hydrus Minimally Invasice [sic; “Invasive”] Glaucoma Surgery (MIGS),” (Hereinafter “MIGS Video”) https://vimeo.com/169867478, at 1:10.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="659 269 1724 784"></div> <p data-bbox="516 841 808 878">(MIGS Video at 1:50.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="682 266 1696 786" data-label="Image"> </div> <p data-bbox="516 841 808 873">(MIGS Video at 2:40.)</p> <ul style="list-style-type: none"> <li data-bbox="567 922 1858 1247"> <p>“The Hydrus Microstent is an ab interno canal-based MIGS approach designed to optimize aqueous drainage. It is the first device to use a tri-modal mechanism of action to treat areas of resistance that inhibit aqueous flow in the eye. The Hydrus Microstent acts to bypass the obstructed trabecular meshwork by creating an optimal pathway for the aqueous to flow through Schlemm’s canal. Additionally, with its open scaffold design, the Microstent provides for a gentle dilation of a potentially narrowing or collapsing Schlemm’s canal. And because of its 8-millimeter length and approximate 90-degree span within Schlemm’s canal, the Hydrus allows for enhanced access and unobstructed flow into the numerous collector channels and network of aqueous outflow veins.” (Hydrus Animation at 1:57 – 2:50.)</p> <li data-bbox="567 1287 1837 1354"> <p>“The Hydrus Microstent is designed to reduce intraocular pressure by increasing aqueous flow through Schlemm’s canal, the eye’s natural outflow pathway. The Hydrus Microstent</p>

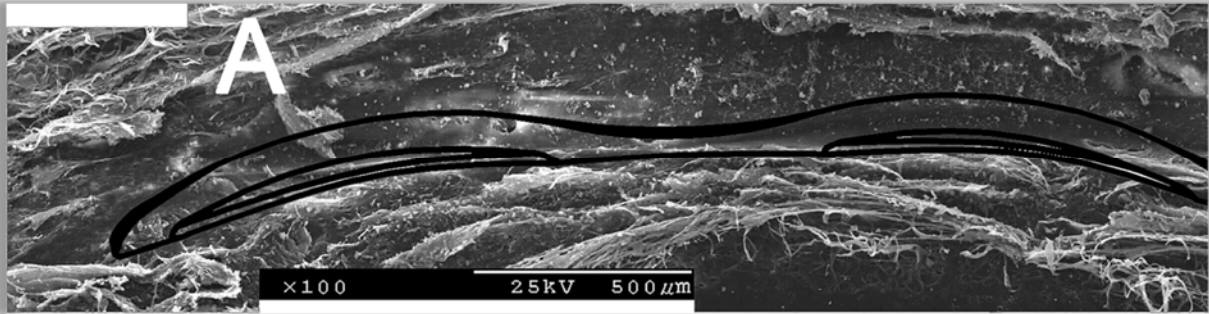
Claim [Limitation]	Evidence of Infringement																														
	<p>restores the flow of fluid in the eye using a trimodal mechanism of action. It creates a bypass through the trabecular meshwork allowing flow from the anterior chamber into Schlemm’s canal. The Hydrus Microstent scaffolds the canal, expanding the natural diameter to augment flow. It’s length spans approximately 90 degrees of the canal, to provide access to the fluid collector channels in the eye.” (Hydrus Animation at 5:52 - 6:35.)</p>  <p>Figure 3 is a line graph showing Outflow Facility (μl/min/mmHg) on the Y-axis (ranging from 0.10 to 0.55) versus Perfusion IOP (mmHg) on the X-axis (ranging from 10 to 50). The graph compares four conditions: Baseline (Receiving Hydrus) (dashed line with open triangles), Baseline (Receiving iStents) (dashed line with open squares), Hydrus (solid line with solid triangles), and iStents (solid line with solid squares). Error bars represent SEM. Asterisks (*) indicate P < 0.05 for scaffold versus baseline 1. A dagger (†) indicates P < 0.05 for two micro-bypasses versus baseline 2. A bracket labeled NS indicates that baseline measurements from contralateral eyes were not significantly different.</p> <table border="1"><thead><tr><th>Perfusion IOP (mmHg)</th><th>Baseline (Receiving Hydrus) (μl/min/mmHg)</th><th>Baseline (Receiving iStents) (μl/min/mmHg)</th><th>Hydrus (μl/min/mmHg)</th><th>iStents (μl/min/mmHg)</th></tr></thead><tbody><tr><td>10</td><td>~0.34</td><td>~0.28</td><td>~0.45</td><td>~0.37</td></tr><tr><td>20</td><td>~0.27</td><td>~0.30</td><td>~0.41</td><td>~0.35</td></tr><tr><td>30</td><td>~0.28</td><td>~0.31</td><td>~0.46</td><td>~0.38</td></tr><tr><td>40</td><td>~0.24</td><td>~0.26</td><td>~0.47</td><td>~0.38</td></tr><tr><td>50</td><td>~0.25</td><td>~0.29</td><td>~0.41</td><td>~0.35</td></tr></tbody></table> <p>FIGURE 3. Calculated outflow facilities (C) for anterior segments with implanted scaffold or two micro-bypasses. Bars represent SEM. *$P < 0.05$ for scaffold versus baseline 1. †$P < 0.05$ for two micro-bypasses versus baseline 2. Baseline measurements from contralateral eyes were not significantly different (NS).</p>	Perfusion IOP (mmHg)	Baseline (Receiving Hydrus) (μl/min/mmHg)	Baseline (Receiving iStents) (μl/min/mmHg)	Hydrus (μl/min/mmHg)	iStents (μl/min/mmHg)	10	~0.34	~0.28	~0.45	~0.37	20	~0.27	~0.30	~0.41	~0.35	30	~0.28	~0.31	~0.46	~0.38	40	~0.24	~0.26	~0.47	~0.38	50	~0.25	~0.29	~0.41	~0.35
Perfusion IOP (mmHg)	Baseline (Receiving Hydrus) (μl/min/mmHg)	Baseline (Receiving iStents) (μl/min/mmHg)	Hydrus (μl/min/mmHg)	iStents (μl/min/mmHg)																											
10	~0.34	~0.28	~0.45	~0.37																											
20	~0.27	~0.30	~0.41	~0.35																											
30	~0.28	~0.31	~0.46	~0.38																											
40	~0.24	~0.26	~0.47	~0.38																											
50	~0.25	~0.29	~0.41	~0.35																											

Claim [Limitation]	Evidence of Infringement																																																																							
	<p>(Cassandra L. Hays et al., “Improvement in Outflow Facility by Two Novel Microinvasive Glaucoma Surgery Implants,” 55:3 INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCI. 1893, 1896 (2014) (hereinafter “Hays”).)</p> <p>TABLE 2. Summary of Outflow Facilities Before and After Device Implantation</p> <table><tr><th rowspan="2">PP, mm Hg</th><th colspan="4">Scaffold</th><th colspan="4">2 Micro-Bypasses</th></tr><tr><th>Pre</th><th>Post</th><th>Change</th><th>P</th><th>Pre</th><th>Post</th><th>Change</th><th>P</th></tr><tr><td>10</td><td>0.34 ± 0.19</td><td>0.45 ± 0.19</td><td>0.07 ± 0.12</td><td>0.053</td><td>0.29 ± 0.14</td><td>0.37 ± 0.12</td><td>0.09 ± 0.16</td><td>0.09</td></tr><tr><td>20</td><td>0.28 ± 0.08</td><td>0.41 ± 0.13</td><td>0.13 ± 0.13</td><td>0.003</td><td>0.30 ± 0.13</td><td>0.35 ± 0.11</td><td>0.05 ± 0.15</td><td>0.27</td></tr><tr><td>30</td><td>0.28 ± 0.11</td><td>0.46 ± 0.15</td><td>0.18 ± 0.14</td><td>0.001</td><td>0.31 ± 0.16</td><td>0.39 ± 0.15</td><td>0.08 ± 0.18</td><td>0.17</td></tr><tr><td>40</td><td>0.24 ± 0.12</td><td>0.47 ± 0.17</td><td>0.23 ± 0.14</td><td><0.001</td><td>0.26 ± 0.10</td><td>0.38 ± 0.15</td><td>0.12 ± 0.13</td><td>0.01</td></tr><tr><td>50</td><td>0.25 ± 0.12</td><td>0.41 ± 0.16</td><td>0.16 ± 0.15</td><td>0.003</td><td>0.29 ± 0.09</td><td>0.35 ± 0.16</td><td>0.06 ± 0.11</td><td>0.09</td></tr><tr><td>Mean</td><td>0.28 ± 0.10</td><td>0.44 ± 0.13</td><td>0.16 ± 0.12</td><td>0.001</td><td>0.29 ± 0.09</td><td>0.37 ± 0.12</td><td>0.08 ± 0.12</td><td>0.046</td></tr></table> <p>Data are mean ± SD. Statistical significance between before and after device implantation was determined by paired <i>t</i>-tests. <i>n</i> = 12 pairs. PP, perfusion pressure.</p> <p>(Hays at 1897.)</p> <ul style="list-style-type: none">“Both implants effectively increased C [outflow facility] in human eyes ex vivo. The scaffold increased C by a greater percentage (73% vs. 34%) and at a greater range of perfusion pressures (20 to 50 mm Hg vs. 40 mm Hg) than the two micro-bypasses, suggesting that the 8-mm dilation of Schlemm’s canal by the scaffold may have additional benefits in lowering the outflow resistance. The Hydrus Microstent scaffold may be an effective therapy for increasing outflow facility and thus reducing the IOP in patients with glaucoma.” (Hays at 1893.)	PP, mm Hg	Scaffold				2 Micro-Bypasses				Pre	Post	Change	P	Pre	Post	Change	P	10	0.34 ± 0.19	0.45 ± 0.19	0.07 ± 0.12	0.053	0.29 ± 0.14	0.37 ± 0.12	0.09 ± 0.16	0.09	20	0.28 ± 0.08	0.41 ± 0.13	0.13 ± 0.13	0.003	0.30 ± 0.13	0.35 ± 0.11	0.05 ± 0.15	0.27	30	0.28 ± 0.11	0.46 ± 0.15	0.18 ± 0.14	0.001	0.31 ± 0.16	0.39 ± 0.15	0.08 ± 0.18	0.17	40	0.24 ± 0.12	0.47 ± 0.17	0.23 ± 0.14	<0.001	0.26 ± 0.10	0.38 ± 0.15	0.12 ± 0.13	0.01	50	0.25 ± 0.12	0.41 ± 0.16	0.16 ± 0.15	0.003	0.29 ± 0.09	0.35 ± 0.16	0.06 ± 0.11	0.09	Mean	0.28 ± 0.10	0.44 ± 0.13	0.16 ± 0.12	0.001	0.29 ± 0.09	0.37 ± 0.12	0.08 ± 0.12	0.046
PP, mm Hg	Scaffold				2 Micro-Bypasses																																																																			
	Pre	Post	Change	P	Pre	Post	Change	P																																																																
10	0.34 ± 0.19	0.45 ± 0.19	0.07 ± 0.12	0.053	0.29 ± 0.14	0.37 ± 0.12	0.09 ± 0.16	0.09																																																																
20	0.28 ± 0.08	0.41 ± 0.13	0.13 ± 0.13	0.003	0.30 ± 0.13	0.35 ± 0.11	0.05 ± 0.15	0.27																																																																
30	0.28 ± 0.11	0.46 ± 0.15	0.18 ± 0.14	0.001	0.31 ± 0.16	0.39 ± 0.15	0.08 ± 0.18	0.17																																																																
40	0.24 ± 0.12	0.47 ± 0.17	0.23 ± 0.14	<0.001	0.26 ± 0.10	0.38 ± 0.15	0.12 ± 0.13	0.01																																																																
50	0.25 ± 0.12	0.41 ± 0.16	0.16 ± 0.15	0.003	0.29 ± 0.09	0.35 ± 0.16	0.06 ± 0.11	0.09																																																																
Mean	0.28 ± 0.10	0.44 ± 0.13	0.16 ± 0.12	0.001	0.29 ± 0.09	0.37 ± 0.12	0.08 ± 0.12	0.046																																																																
1[e]: and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C,	<p>The Hydrus Microstent “contacts less than 30% of C,” wherein C is the surface area of a “cylindrical section of the lumen of the canal” in which the support is disposed. Approximately 7mm of the Hydrus Microstent is disposed within Schlemm’s canal once implanted, while an approximately 1mm inlet portion of the Microstent protrudes into Schlemm’s canal:</p>																																																																							

Claim [Limitation]	Evidence of Infringement
the support contacts less than 30% of C.	<div data-bbox="808 272 1570 1161"></div> <p data-bbox="514 1222 1860 1294">The 7mm portion of the Hydrus Microstent disposed within Schlemm's canal is comprised of a three "window regions," three "spine regions," and one "inlet spine region." According to the below figures,</p>

Claim [Limitation]	Evidence of Infringement																																																																																																																																							
	each window region spans 1.1 mm, each spine region spans 0.9 mm, and the inlet spine region spans 1.1 mm, for a total length of 7.1 mm:																																																																																																																																							
	<table><tr><th colspan="4">TABLE 1. Geometric Parameters of Implants</th></tr><tr><th>Parameters</th><th>Description</th><th>Value</th><th>Source</th></tr><tr><td colspan="4">8-mm scaffold</td></tr><tr><td>A_w</td><td>Area of window region</td><td>17553 μm^2</td><td>Ivantis</td></tr><tr><td>A_s</td><td>Area of spine region</td><td>22955 μm^2</td><td>Ivantis</td></tr><tr><td>A_{in}</td><td>Area of inlet spine region</td><td>29841 μm^2</td><td>Ivantis</td></tr><tr><td>h_w</td><td>Height of window region</td><td>76.3 μm</td><td>A_w/w_d</td></tr><tr><td>h_s</td><td>Height of spine region</td><td>99.8 μm</td><td>A_s/w_d</td></tr><tr><td>h_{in}</td><td>Height of inlet spine region</td><td>129.7 μm</td><td>A_{in}/w_d</td></tr><tr><td>L_w</td><td>Length of window region</td><td>1.1 mm</td><td>Ivantis</td></tr><tr><td>N_w</td><td>No. windows</td><td>3</td><td>Ivantis</td></tr><tr><td>w_d</td><td>Width of device</td><td>230 μm</td><td>Assumption</td></tr><tr><td>L_{in}</td><td>Length of inlet spine region</td><td>1.1 mm</td><td>Ivantis</td></tr><tr><td>L_{dev}</td><td>Length of device</td><td>7.2 mm</td><td>Ivantis</td></tr><tr><td>L_s</td><td>Length of spine region</td><td>0.9 mm</td><td>Ivantis</td></tr><tr><td colspan="4">15-mm scaffold</td></tr><tr><td>A_w</td><td>Area in window region</td><td>20994 μm^2</td><td>Ivantis</td></tr><tr><td>A_s</td><td>Area in device region</td><td>32092 μm^2</td><td>Ivantis</td></tr><tr><td>A_{in}</td><td>Area of inlet spine region</td><td>29841 μm^2</td><td>Ivantis</td></tr><tr><td>h_w</td><td>Height of window region</td><td>91.3 μm</td><td>A_w/w_d</td></tr><tr><td>h_s</td><td>Height of spine region</td><td>139.5 μm</td><td>A_s/w_d</td></tr><tr><td>h_{in}</td><td>Height of inlet spine region</td><td>129.7 μm</td><td>A_{in}/w_d</td></tr><tr><td>L_w</td><td>Length of window region</td><td>1 mm</td><td>Ivantis</td></tr><tr><td>N_w</td><td>No. windows</td><td>5</td><td>Ivantis</td></tr><tr><td>w_d</td><td>Width of device</td><td>230 μm</td><td>Assumption</td></tr><tr><td>L_{in}</td><td>Length of inlet spine region</td><td>1.1 mm</td><td>Ivantis</td></tr><tr><td>L_{dev}</td><td>Length of device</td><td>15 mm</td><td>Ivantis</td></tr><tr><td>L_s</td><td>Length of spine region</td><td>1.5 mm</td><td>Ivantis</td></tr><tr><td colspan="4">Trabecular microbypass</td></tr><tr><td>A_s</td><td>Area of device</td><td>5652 μm^2</td><td>$\pi 60^2/2$; cross-section is a half-circle with diameter of 120 μm¹⁹</td></tr><tr><td>h_s</td><td>Height of device</td><td>25.0 μm</td><td>A_s/w_d</td></tr><tr><td>w_d</td><td>Width of device</td><td>230 μm</td><td>Assumption</td></tr><tr><td>L_{dev}</td><td>Length of device</td><td>1.0 mm</td><td>Samuelson et al¹⁹</td></tr></table>				TABLE 1. Geometric Parameters of Implants				Parameters	Description	Value	Source	8-mm scaffold				A_w	Area of window region	17553 μm^2	Ivantis	A_s	Area of spine region	22955 μm^2	Ivantis	A_{in}	Area of inlet spine region	29841 μm^2	Ivantis	h_w	Height of window region	76.3 μm	A_w/w_d	h_s	Height of spine region	99.8 μm	A_s/w_d	h_{in}	Height of inlet spine region	129.7 μm	A_{in}/w_d	L_w	Length of window region	1.1 mm	Ivantis	N_w	No. windows	3	Ivantis	w_d	Width of device	230 μm	Assumption	L_{in}	Length of inlet spine region	1.1 mm	Ivantis	L_{dev}	Length of device	7.2 mm	Ivantis	L_s	Length of spine region	0.9 mm	Ivantis	15-mm scaffold				A_w	Area in window region	20994 μm^2	Ivantis	A_s	Area in device region	32092 μm^2	Ivantis	A_{in}	Area of inlet spine region	29841 μm^2	Ivantis	h_w	Height of window region	91.3 μm	A_w/w_d	h_s	Height of spine region	139.5 μm	A_s/w_d	h_{in}	Height of inlet spine region	129.7 μm	A_{in}/w_d	L_w	Length of window region	1 mm	Ivantis	N_w	No. windows	5	Ivantis	w_d	Width of device	230 μm	Assumption	L_{in}	Length of inlet spine region	1.1 mm	Ivantis	L_{dev}	Length of device	15 mm	Ivantis	L_s	Length of spine region	1.5 mm	Ivantis	Trabecular microbypass				A_s	Area of device	5652 μm^2	$\pi 60^2/2$; cross-section is a half-circle with diameter of 120 μm ¹⁹	h_s	Height of device	25.0 μm	A_s/w_d	w_d	Width of device	230 μm	Assumption	L_{dev}	Length of device	1.0 mm	Samuelson et al ¹⁹
TABLE 1. Geometric Parameters of Implants																																																																																																																																								
Parameters	Description	Value	Source																																																																																																																																					
8-mm scaffold																																																																																																																																								
A_w	Area of window region	17553 μm^2	Ivantis																																																																																																																																					
A_s	Area of spine region	22955 μm^2	Ivantis																																																																																																																																					
A_{in}	Area of inlet spine region	29841 μm^2	Ivantis																																																																																																																																					
h_w	Height of window region	76.3 μm	A_w/w_d																																																																																																																																					
h_s	Height of spine region	99.8 μm	A_s/w_d																																																																																																																																					
h_{in}	Height of inlet spine region	129.7 μm	A_{in}/w_d																																																																																																																																					
L_w	Length of window region	1.1 mm	Ivantis																																																																																																																																					
N_w	No. windows	3	Ivantis																																																																																																																																					
w_d	Width of device	230 μm	Assumption																																																																																																																																					
L_{in}	Length of inlet spine region	1.1 mm	Ivantis																																																																																																																																					
L_{dev}	Length of device	7.2 mm	Ivantis																																																																																																																																					
L_s	Length of spine region	0.9 mm	Ivantis																																																																																																																																					
15-mm scaffold																																																																																																																																								
A_w	Area in window region	20994 μm^2	Ivantis																																																																																																																																					
A_s	Area in device region	32092 μm^2	Ivantis																																																																																																																																					
A_{in}	Area of inlet spine region	29841 μm^2	Ivantis																																																																																																																																					
h_w	Height of window region	91.3 μm	A_w/w_d																																																																																																																																					
h_s	Height of spine region	139.5 μm	A_s/w_d																																																																																																																																					
h_{in}	Height of inlet spine region	129.7 μm	A_{in}/w_d																																																																																																																																					
L_w	Length of window region	1 mm	Ivantis																																																																																																																																					
N_w	No. windows	5	Ivantis																																																																																																																																					
w_d	Width of device	230 μm	Assumption																																																																																																																																					
L_{in}	Length of inlet spine region	1.1 mm	Ivantis																																																																																																																																					
L_{dev}	Length of device	15 mm	Ivantis																																																																																																																																					
L_s	Length of spine region	1.5 mm	Ivantis																																																																																																																																					
Trabecular microbypass																																																																																																																																								
A_s	Area of device	5652 μm^2	$\pi 60^2/2$; cross-section is a half-circle with diameter of 120 μm ¹⁹																																																																																																																																					
h_s	Height of device	25.0 μm	A_s/w_d																																																																																																																																					
w_d	Width of device	230 μm	Assumption																																																																																																																																					
L_{dev}	Length of device	1.0 mm	Samuelson et al ¹⁹																																																																																																																																					

Claim [Limitation]	Evidence of Infringement
	<p>(Fan Yuan, <i>et al.</i>, “Mathematical Modeling of Outflow Facility Increase with Trabecular Meshwork Bypass and Schlemm Canal Dilation,” 25 J. Glaucoma 355, 358 (2016).)</p> <p>The total surface area of the Hydrus Microstent is 0.057 cm², or 5,700,00 μm² (Srinidhi Nagaraja and Alan R. Pelton, <i>Corrosion resistance of a Nitinol ocular microstent: Implications on biocompatibility</i>, J. Biomed Mater Res. 108B:2681-2690 (2020).)</p> <p>Using dimensions and surface area figures reported by Yuan, et al., and Nagaraja and Pelton, the surface area of the Hydrus Microstent that potentially might contact the interior wall of Schlemm’s canal can be calculated as the total surface area (5,700,000 μm²), minus the area of the inlet portion that resides in the anterior chamber (60% of the lateral area of a cylinder with a radius of 146 μm and length of 900 μm), minus the outside edge area (60 μm * 16750μm), minus the window edge area (60 μm * 3 * circumference of an oval of length 1100 μm and height of 200 μm), minus the inlet spine second edge area (60 μm * 2200 μm), divided in half. The resulting surface area that could potentially contact Schlemm’s canal is approximately 1,793,871 μm² which is less than 30% of a 7.1 mm cylinder with a radius of 146 μm.</p> <p>Furthermore, because the Hydrus Microstent makes only discontinuous contact with Schlemm’s canal, the potential area of contact is substantially less than 1,793,871 μm².</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="537 266 1738 578"></div> <p data-bbox="516 602 1837 672">(Johnstone et al., “Effects of a Schlemm Canal Scaffold on Collector Channel Ostia in Human Anterior Segments,” 119 Experimental Eye Research 70 (2014).)</p> <p data-bbox="516 712 1852 782">Specifically, while the window regions of the Hydrus scaffold and dilate the canal, the areas between the window regions have limited contact with the canal wall.</p>

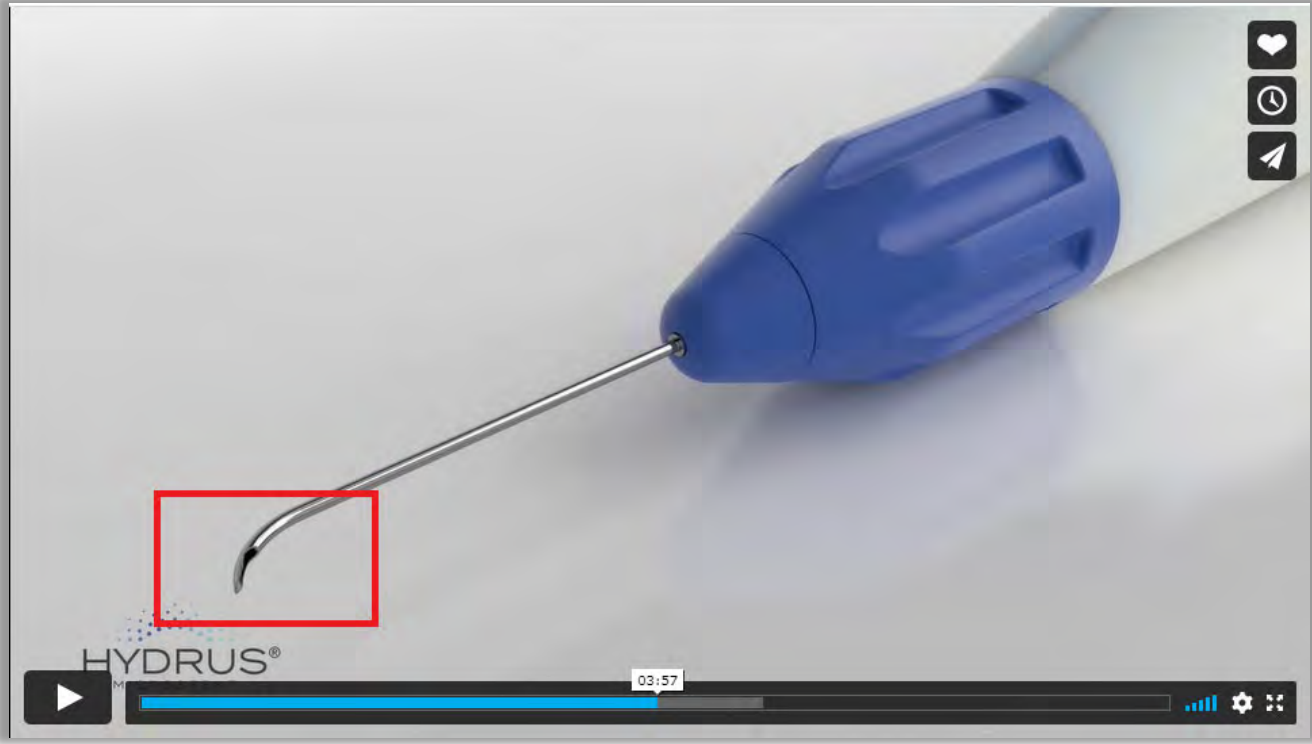
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="720 269 1654 967" data-label="Image"> </div> <p data-bbox="514 1027 1837 1097">(Saba Samet, et al., <i>Hydrus microstent implantation for surgical management of glaucoma: a review of design, efficacy and safety</i>, Eye and Vision, Vol. 6, No. 32 (2019).)</p> <p data-bbox="514 1138 1837 1243">The Hydrus Microstent IFU and promotional materials additionally confirm that the Hydrus Microstent is designed so as to minimize surface area contact between the implant and the interior wall of Schlemm's canal, so as to maximize open flow of aqueous humor across and through the canal.</p> <ul data-bbox="562 1284 1816 1354" style="list-style-type: none"> • “The microstent is approximately 8mm in overall length with major and minor axes of 292μm and 185μm, respectively. The length and curvature of the implant are designed to occupy

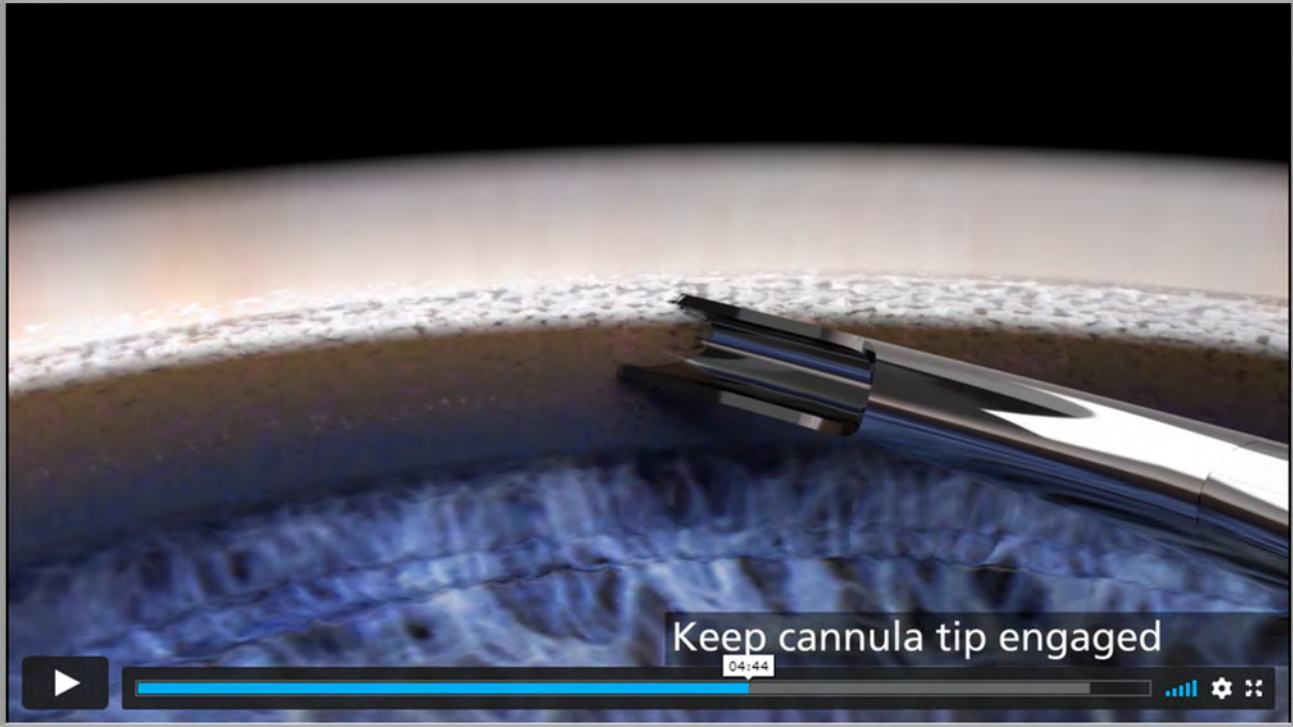
Claim [Limitation]	Evidence of Infringement
	<p>approximately 90° or 3 clock hours of Schlemm’s canal. The implant is designed to have adequate structural thickness to support the tissue of the canal while providing maximum open flow areas through the canal, with the proximal portion of the implant exiting the canal through the trabecular meshwork to allow inflow of aqueous humor from the anterior chamber.” (IFU at 1.)</p> <ul style="list-style-type: none"> • “The Hydrus Microstent is an ab interno canal-based MIGS approach designed to optimize aqueous drainage. It is the first device to use a tri-modal mechanism of action to treat areas of resistance that inhibit aqueous flow in the eye. The Hydrus Microstent acts to bypass the obstructed trabecular meshwork by creating an optimal pathway for the aqueous to flow through Schlemm’s canal. Additionally, with its open scaffold design, the Microstent provides for a gentle dilation of a potentially narrowing or collapsing Schlemm’s canal. And because of its 8-millimeter length and approximate 90-degree span within Schlemm’s canal, the Hydrus allows for enhanced access and unobstructed flow into the numerous collector channels and network of aqueous outflow veins.” (Hydrus Animation at 1:57 – 2:50.)

EXHIBIT N

Exemplary Claim Chart of Hydrus® Microstent Against U.S. Patent No. 9,486,361 (“’361 Patent”)

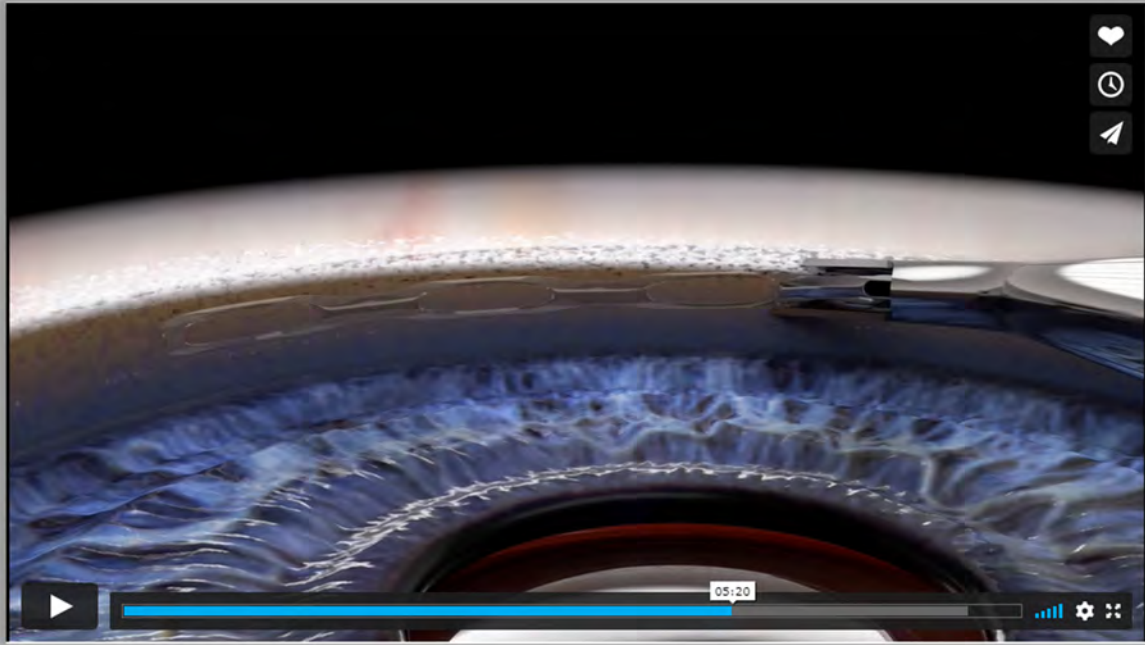
Claim [Limitation]	Evidence of Infringement
1[pre]: A method for reducing intraocular pressure, comprising:	<p>The Hydrus Microstent implantation procedure is a “method for reducing intraocular pressure”:</p> <ul style="list-style-type: none"> • “Ivantis, a company dedicated to the development of innovative solutions for glaucoma therapy brings you the Hydrus Microstent, a groundbreaking MIGS technology designed to relieve the high intraocular pressure of the eye that is common in patients with primary open angle glaucoma.” (“IM-00 16-1-2 Rev B OUS Hydrus Microstent Animation (Full)”, https://vimeo.com/510821860 (hereinafter “Hydrus Animation”) at 1:35 – 1:55.) • “The Hydrus Microstent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG).” (Hydrus Microstent Instructions for Use (hereinafter “IFU”), at 3.)
1[a]: introducing a tubular cannula having a lumen at least partially within Schlemm’s canal;	<p>The Hydrus Microstent implantation procedure involves “introducing a tubular cannula having a lumen at least partially within Schlemm’s canal”:</p> <ul style="list-style-type: none"> • “The microstent is implanted into the eye using a hand-held delivery system (Figure 2) that provides for delivery of the implant through a stainless steel cannula into the target site in the eye. The delivery system was designed to provide smooth tracking and controlled delivery of the microstent into Schlemm's canal. The delivery system is an ergonomic design for use in either the right or left hand, allowing for surgeon individual preference and hand position. To accommodate a wide range of hand positions, a rotatable sleeve at the distal end allows positioning and alignment of the cannula by the surgeon to direct the implant into Schlemm's canal. The tracking wheel on the delivery system serves as the control mechanism to advance the implant into the canal or retract the implant into the cannula. To deliver the microstent into Schlemm’s canal, the cannula of the delivery system is inserted through a clear corneal incision (approximately 1.5 mm in length). The cannula tip is then advanced through the trabecular meshwork until it enters Schlemm’s canal and the entry point into

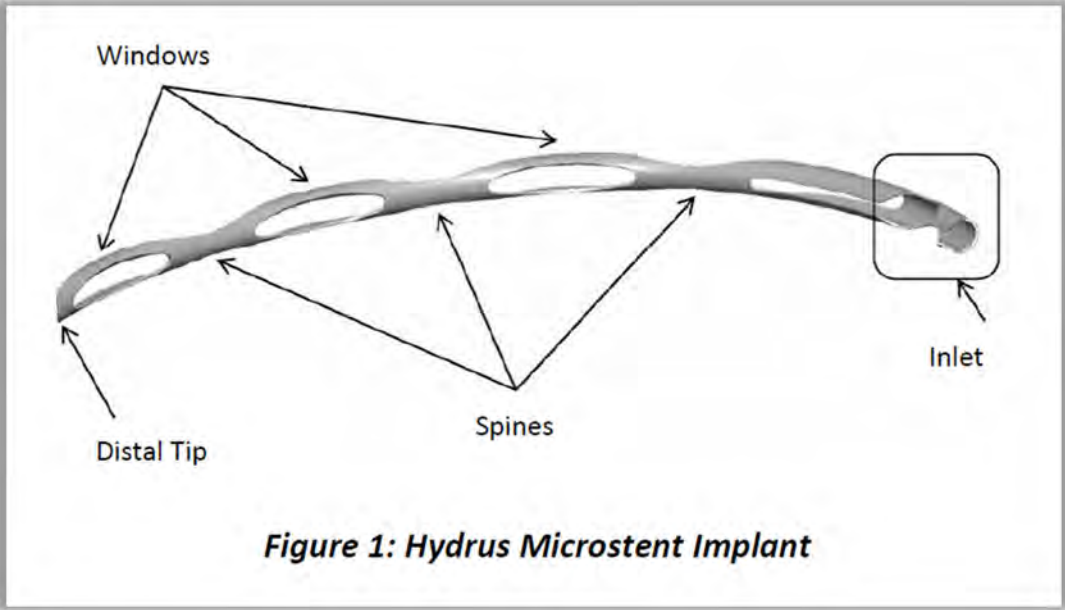
Claim [Limitation]	Evidence of Infringement
	<p data-bbox="606 235 1860 378">the meshwork is coincident with the end of the cannula bevel. The target tissue is visualized using a gonioscopic prism. After observing that the distal cannula tip is properly positioned through the trabecular meshwork into Schlemm's canal, the tracking wheel on the delivery system is used to advance and release the microstent.” (IFU at 2-3.)</p> <div data-bbox="533 435 1837 1174"></div> <p data-bbox="514 1230 1627 1268">(Hydrus Animation at 3:57 (red box added for emphasis to identify lumen of cannula).)</p>

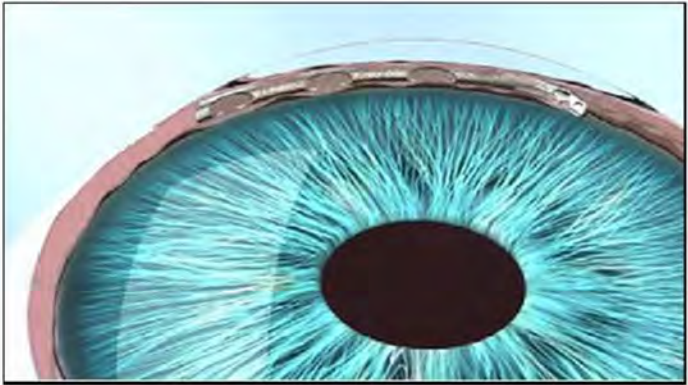
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="533 253 1818 976">  </div> <p data-bbox="512 1036 877 1068">(Hydrus Animation at 4:44.)</p> <ul data-bbox="562 1110 1856 1362" style="list-style-type: none"> • “The Hydrus cannula is inserted through a corneal incision at the temporal position and directed towards the trabecular meshwork where it is positioned parallel to Schlemm’s canal. Under gonioscopy, the beveled tip of the cannula should be tilted up approximately fifteen degrees, and then used to access Schlemm’s canal through the trabecular meshwork just above the scleral spur. Once through the trabecular meshwork, hold the cannula steady with light contact against the back wall of Schlemm’s canal. Begin to deliver the Hydrus by gently rolling the tracking wheel forward while keeping the cannula tip engaged. Continue to advance the Hydrus

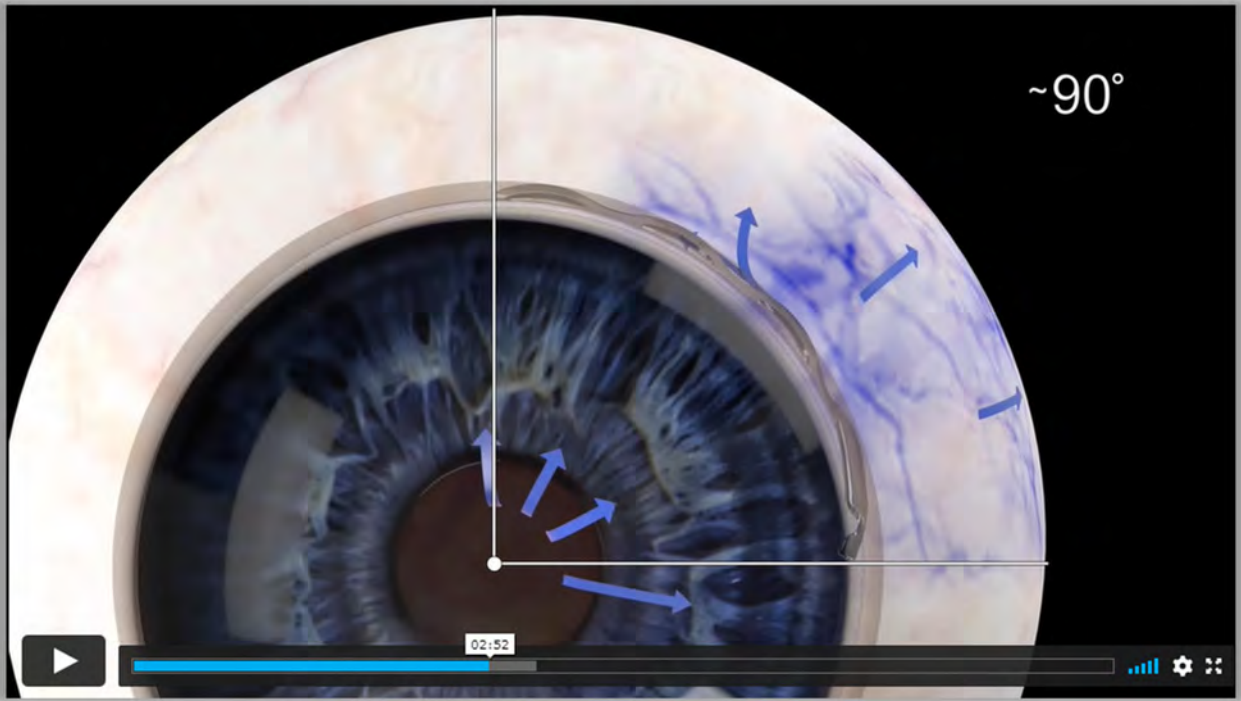
Claim [Limitation]	Evidence of Infringement
	<p>with a slow and steady motion while gently relaxing the upward and forward pressure on the cannula.” (Hydrus Animation at 4:05 – 4:56.)</p>
<p>1[b]: delivering a high viscosity fluid into Schlemm’s canal; and</p>	<p>On information and belief, Ivantis and its agents recently began promoting the Hydrus® Microstent for use in combination with certain viscoelastic delivery cannulas, with Ivantis sales representatives and agents providing instructions to surgeons and facilities to first perform viscoelastic delivery within Schlemm’s canal, i.e., “canaloplasty,” in advance of delivering the Hydrus® Microstent. One such individual who has actively promoted this procedure is Andy Rivero, of Vero Beach, Florida.</p> <p>When used in combination with said viscoelastic delivery cannulas, the Hydrus Microstent implantation procedure involves “delivering a high viscosity fluid,” such as viscoelastic, “into Schlemm’s canal.”</p>
<p>1[c]: inserting a support into Schlemm’s canal by passing the support through the tubular cannula, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than a radius of curvature of Schlemm’s canal, and wherein the support comprises at least one fenestration.</p>	<p>The Hydrus Microstent is a “support.”</p> <ul style="list-style-type: none"> • “The microstent (Figure 1) is composed of nitinol, a metal alloy of nickel (Ni) and titanium (Ti). Nitinol has been used extensively in a variety of implantable devices for its proven properties of flexibility, strength and biocompatibility. As a shape memory alloy, nitinol has super-elastic properties making it suitable as a support structure in Schlemm's canal. The implant is laser cut from nitinol tubing to a proprietary design with alternating “spines” for structural support and “windows” to provide outflow pathways for aqueous humor. After laser cutting, the shape of the implant is heat-set to a curvature that matches the curvature of Schlemm’s canal and is electro-polished to create a smooth biocompatible surface. The microstent is approximately 8mm in overall length with major and minor axes of 292µm and 185µm, respectively. The length and curvature of the implant are designed to occupy approximately 90° or 3 clock hours of Schlemm’s canal. The implant is designed to have adequate structural thickness to support the tissue of the canal while providing maximum open flow areas through the canal, with the proximal portion of the implant exiting the canal through the trabecular meshwork to allow inflow of aqueous humor from the anterior chamber.” (IFU at 1.)


Claim [Limitation]	Evidence of Infringement
	<p data-bbox="512 235 1864 305">The Hydrus Microstent implantation procedure involves “inserting a support into Schlemm’s canal by passing the support through the tubular cannula”:</p> <div data-bbox="537 358 1696 1015"></div> <p data-bbox="512 1073 877 1109">(Hydrus Animation at 4:58.)</p>

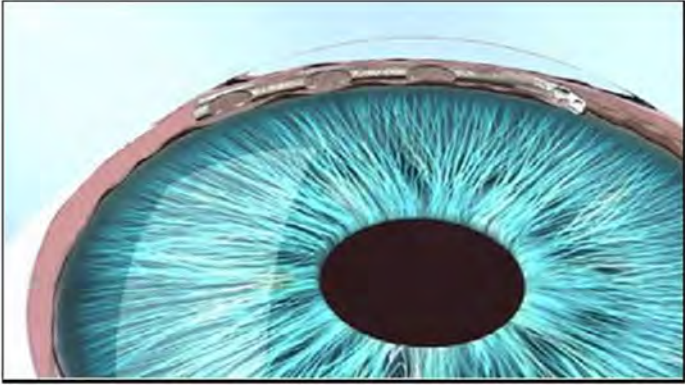
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="537 248 1675 889"></div> <p data-bbox="512 946 877 979">(Hydrus Animation at 5:20.)</p> <ul data-bbox="562 1024 1856 1276" style="list-style-type: none">• “The Hydrus highly flexible rounded frame design provides for a smooth passage into Schlemm’s canal. Observing the first window of the Hydrus as it enters Schlemm’s canal will provide verification that the device is being delivered properly. You’ll notice how the translucency of the trabecular meshwork causes the Hydrus to appear less shiny as it is delivered. Once satisfied with its position, the Hydrus is advanced until the microstent is released from the interlock. The Hydrus cannula is then removed from Schlemm’s canal and withdrawn from the eye.” (Hydrus Animation, 4:55 - 5:35.)

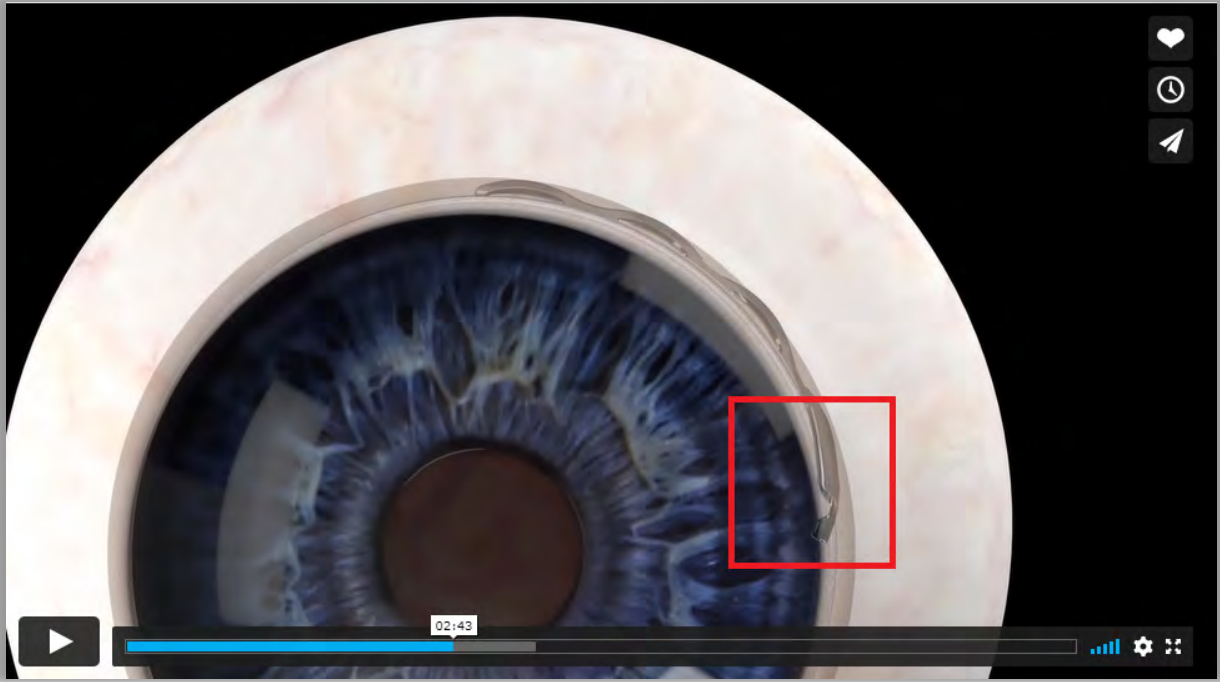
Claim [Limitation]	Evidence of Infringement
	<p data-bbox="562 237 909 264"><i>See also</i> claim 1[b], above.</p> <p data-bbox="516 310 1247 337">The Hydrus Microstent comprises an “arcuate member”</p> <div data-bbox="533 391 1591 997"><p data-bbox="793 919 1339 946">Figure 1: Hydrus Microstent Implant</p></div> <p data-bbox="516 1057 653 1084">(IFU at 1.)</p>

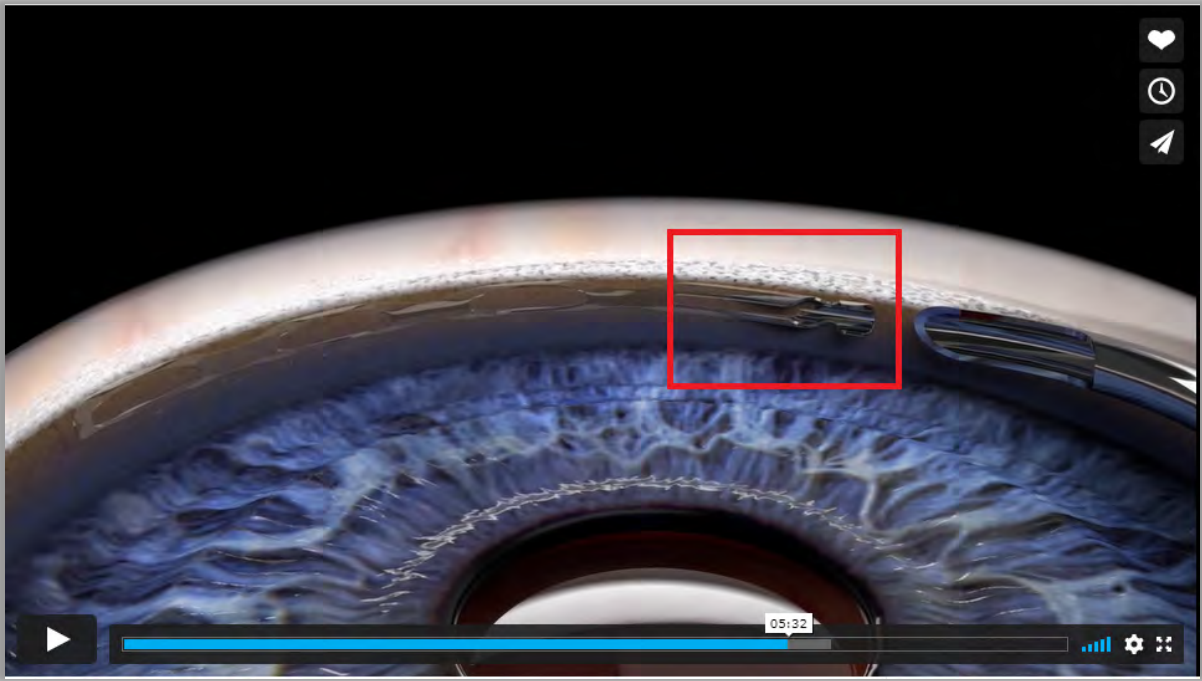
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="802 267 1486 649"></div> <p data-bbox="562 695 1726 782"><i>Figure 5: Microstent in Schlemm's Canal</i> (Proximal end at right accessing aqueous humor from the anterior chamber)</p> <p data-bbox="514 865 651 901">(IFU at 8.)</p>

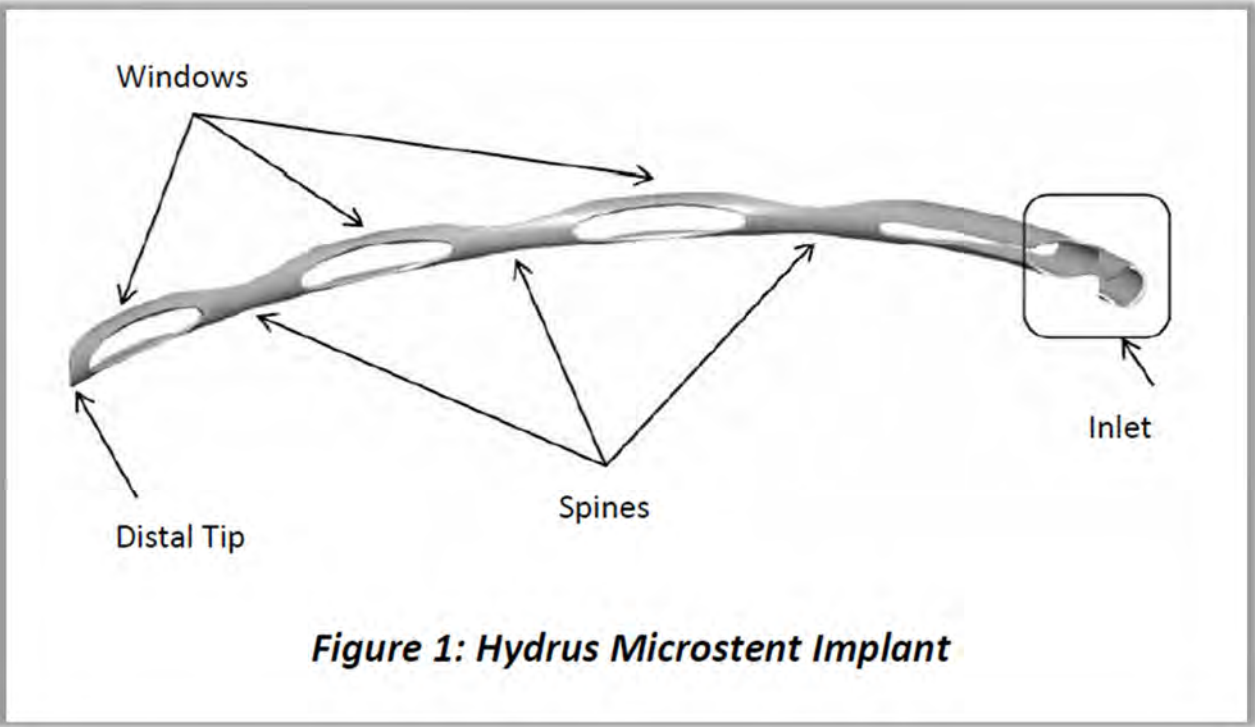
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="533 250 1766 946"></div> <p data-bbox="512 1003 877 1040">(Hydrus Animation at 2:52.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="525 243 1795 966"></div> <p data-bbox="512 1019 877 1052">(Hydrus Animation at 6:44.)</p> <p data-bbox="512 1094 1835 1234">At least a “portion” of the Hydrus Microstent has “a radius of curvature smaller than a radius of curvature of Schlemm’s canal.” Specifically, once implanted, the overall radius of the Hydrus Microstent is smaller than that of Schlemm’s canal, as evidenced by the fact that it protrudes at one end out of Schlemm’s canal and into the anterior chamber.</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="583 245 1793 813"><p data-bbox="604 699 1772 781"><i>Figure 5: Microstent in Schlemm's Canal</i> (Proximal end at right accessing aqueous humor from the anterior chamber)</p></div> <p data-bbox="512 870 651 902">(IFU at 8.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="533 253 1745 930"></div> <p data-bbox="512 987 1260 1027">(Hydrus Animation at 2:43 (red box added for emphasis).)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="592 250 1787 927">A video frame showing a cross-section of a medical device, likely a catheter or probe, with a red box highlighting a specific feature. The device has a blue, textured outer layer and a white, curved inner layer. The highlighted area shows a small, dark, rectangular opening or fenestration in the white layer. The video player interface at the bottom shows a play button, a progress bar, and a timestamp of 05:32.</div> <p data-bbox="512 987 877 1024">(Hydrus Animation at 5:32.)</p> <p data-bbox="512 1060 1276 1097">Finally, the support “comprises at least one fenestration”:</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="533 245 1780 967"><p>The diagram illustrates a Hydrus Microstent Implant, which is a curved, elongated device. It features several oval-shaped openings along its length, labeled 'Windows'. The device tapers to a 'Distal Tip' on the left and has an 'Inlet' at the right end, which is shown in a magnified view. 'Spines' are indicated as the structural ridges between the windows. The caption below the diagram reads 'Figure 1: Hydrus Microstent Implant'.</p></div> <p data-bbox="514 1024 1354 1062">(Hydrus Microstent Instructions for Use (hereinafter “IFU”) at 2.)</p>

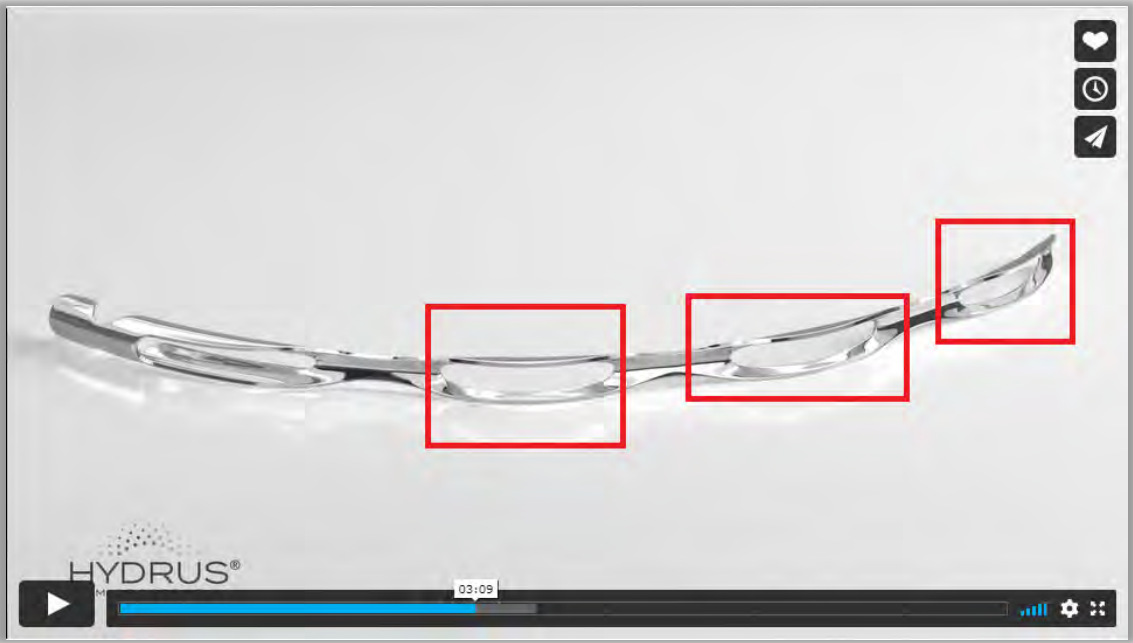
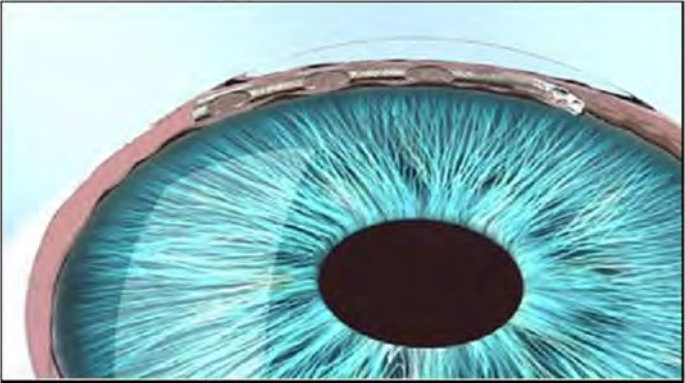
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="625 245 1751 883"></div> <p data-bbox="512 938 877 976">(Hydrus Animation at 3:09.)</p>


EXHIBIT O

Exemplary Claim Chart of Hydrus® Microstent Against U.S. Patent No. 10,314,742 (“742 Patent”)

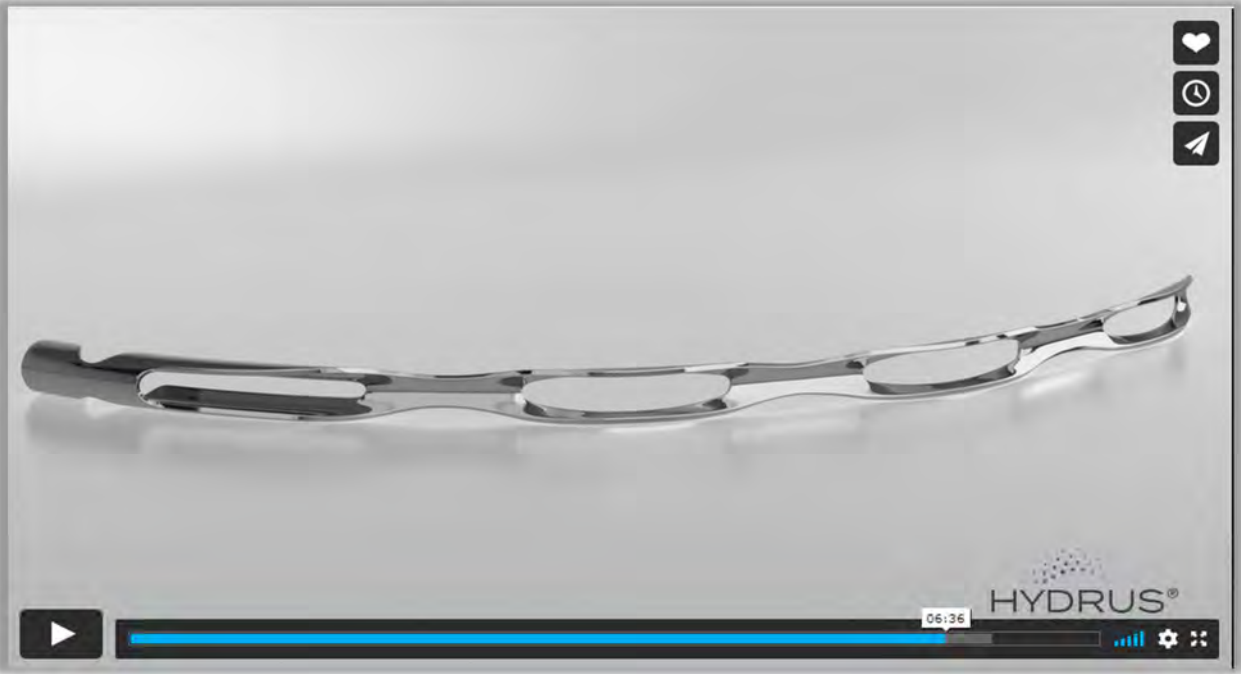
Claim [Limitation]	Evidence of Infringement
1[pre]: A method for treating an eye condition, comprising:	<p>The Hydrus Microstent implantation procedure is a “method for treating an eye condition”:</p> <ul style="list-style-type: none"> • “Ivantis, a company dedicated to the development of innovative solutions for glaucoma therapy brings you the Hydrus Microstent, a groundbreaking MIGS technology designed to relieve the high intraocular pressure of the eye that is common in patients with primary open angle glaucoma.” (“IM-00 16-1-2 Rev B OUS Hydrus Microstent Animation (Full)”, https://vimeo.com/510821860 (hereinafter “Hydrus Animation”) at 1:35 – 1:55.) • “The Hydrus Microstent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG).” (Hydrus Microstent Instructions for Use (hereinafter “IFU”), at 3.)
1[a]: implanting a support within Schlemm’s canal, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than the radius of curvature of Schlemm’s canal such that at least a portion of the	<p>The Hydrus Microstent is a “support”:</p> <ul style="list-style-type: none"> • “The microstent (Figure 1) is composed of nitinol, a metal alloy of nickel (Ni) and titanium (Ti). Nitinol has been used extensively in a variety of implantable devices for its proven properties of flexibility, strength and biocompatibility. As a shape memory alloy, nitinol has super-elastic properties making it suitable as a support structure in Schlemm's canal. The implant is laser cut from nitinol tubing to a proprietary design with alternating “spines” for structural support and “windows” to provide outflow pathways for aqueous humor. After laser cutting, the shape of the implant is heat-set to a curvature that matches the curvature of Schlemm’s canal and is electro-polished to create a smooth biocompatible surface. The microstent is approximately 8mm in overall length with major and minor axes of 292µm and 185µm, respectively. The length and curvature of the implant are designed to occupy approximately 90° or 3 clock hours of Schlemm’s canal. The implant is designed to have adequate structural thickness to support the tissue of the canal while providing maximum open flow areas through the canal, with the proximal portion of the


Claim [Limitation]	Evidence of Infringement
<p>arcuate member extends out of Schlemm's canal.</p>	<p>implant exiting the canal through the trabecular meshwork to allow inflow of aqueous humor from the anterior chamber.” (IFU at 1.)</p> <p>The Hydrus Microstent implantation procedure involves “implanting a support within Schlemm’s canal”:</p> <ul style="list-style-type: none"> • “The microstent is implanted into the eye using a hand-held delivery system (Figure 2) that provides for delivery of the implant through a stainless steel cannula into the target site in the eye. The delivery system was designed to provide smooth tracking and controlled delivery of the microstent into Schlemm's canal. The delivery system is an ergonomic design for use in either the right or left hand, allowing for surgeon individual preference and hand position. To accommodate a wide range of hand positions, a rotatable sleeve at the distal end allows positioning and alignment of the cannula by the surgeon to direct the implant into Schlemm's canal. The tracking wheel on the delivery system serves as the control mechanism to advance the implant into the canal or retract the implant into the cannula. To deliver the microstent into Schlemm’s canal, the cannula of the delivery system is inserted through a clear corneal incision (approximately 1.5 mm in length). The cannula tip is then advanced through the trabecular meshwork until it enters Schlemm’s canal and the entry point into the meshwork is coincident with the end of the cannula bevel. The target tissue is visualized using a gonioscopic prism. After observing that the distal cannula tip is properly positioned through the trabecular meshwork into Schlemm's canal, the tracking wheel on the delivery system is used to advance and release the microstent.” (IFU at 2-3.)

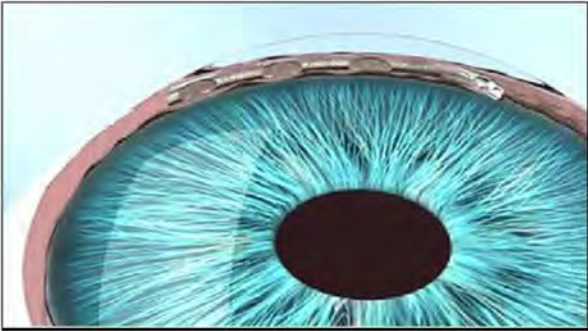
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="573 284 1787 846"><p data-bbox="596 735 1764 816"><i>Figure 5: Microstent in Schlemm's Canal</i> (Proximal end at right accessing aqueous humor from the anterior chamber)</p></div> <p data-bbox="485 906 621 938">(IFU at 8.)</p>

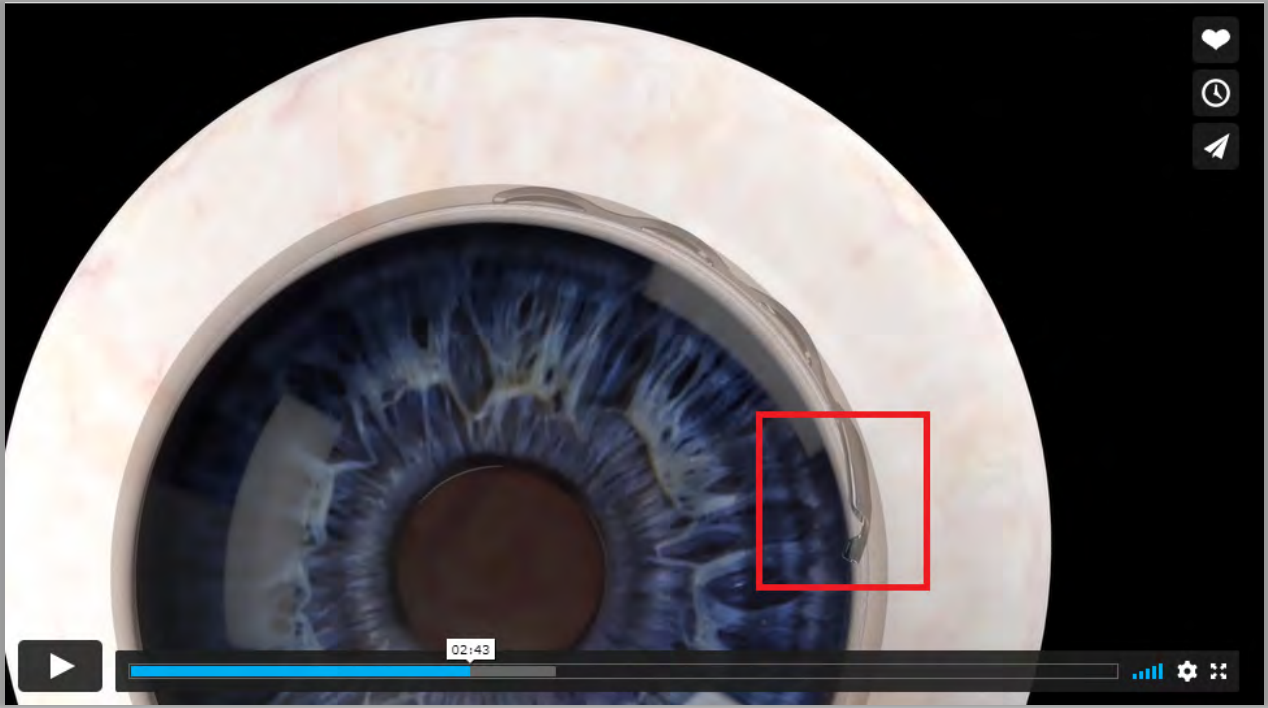
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="569 289 1787 971"></div> <p data-bbox="485 1031 850 1063">(Hydrus Animation at 5:40.)</p> <ul data-bbox="533 1109 1839 1323" style="list-style-type: none">• “The Hydrus cannula is inserted through a corneal incision at the temporal position and directed towards the trabecular meshwork where it is positioned parallel to Schlemm’s canal. Under gonioscopy, the beveled tip of the cannula should be tilted up approximately fifteen degrees, and then used to access Schlemm’s canal through the trabecular meshwork, just above the scleral spur. Once through the trabecular meshwork, hold the cannula steady with light contact against the back wall of Schlemm’s canal.” (Hydrus Animation at 4:05 – 4:40.)

Claim [Limitation]	Evidence of Infringement
	<ul style="list-style-type: none"><li data-bbox="533 272 1879 597">• “Begin to deliver the Hydrus by gently rolling the tracking wheel forward while keeping the cannula tip engaged. Continue to advance the Hydrus with a slow and steady motion while gently relaxing the upward and forward pressure on the cannula. The Hydrus highly flexible rounded frame design provides for a smooth passage into Schlemm’s canal. Observing the first window of the Hydrus as it enters Schlemm’s canal will provide verification that the device is being delivered properly. You’ll notice how the translucency of the trabecular meshwork causes the Hydrus to appear less shiny as it is delivered. Once satisfied with its position, the Hydrus is advanced until the microstent is released from the interlock. The Hydrus cannula is then removed from Schlemm’s canal and withdrawn from the eye.” (Hydrus Animation at 4:40 – 5:38.) <p data-bbox="485 639 1073 672">The support comprises an “arcuate member”</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="512 282 1745 951"></div> <p data-bbox="485 1003 850 1040">(Hydrus Animation at 6:36.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="499 280 1822 1036"></div> <p data-bbox="489 1092 850 1128">(Hydrus Animation at 6:44.)</p> <p data-bbox="489 1166 1877 1273">At least a portion of the arcuate member, i.e. the Hydrus Microstent, has a “radius smaller than the radius of the curvature of Schlemm’s canal.” Specifically, once implanted, the overall radius of the Hydrus Microstent is smaller than that of Schlemm’s canal, as evidenced by the fact that it protrudes at one end out</p>

Claim [Limitation]	Evidence of Infringement
	<p data-bbox="485 272 1850 342">of Schlemm's canal and into the anterior chamber. Thus, at least “a portion of the arcuate member,” i.e. the Hydrus Microstent, “extends out of Schlemm's canal”:</p> <div data-bbox="512 396 1843 1068"><p data-bbox="527 415 1808 488">Figure 5 shows the microstent positioned in Schlemm's canal with the proximal end (i.e., the inlet) protruding slightly into the anterior chamber for inflow of aqueous humor.</p><p data-bbox="688 935 1696 1008">Figure 5: Microstent in Schlemm's Canal (Proximal end at right accessing aqueous humor from the anterior chamber)</p></div> <p data-bbox="485 1130 621 1162">(IFU at 8.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="548 289 1808 992"></div> <p data-bbox="485 1052 1230 1089">(Hydrus Animation at 2:43 (red box added for emphasis).)</p>

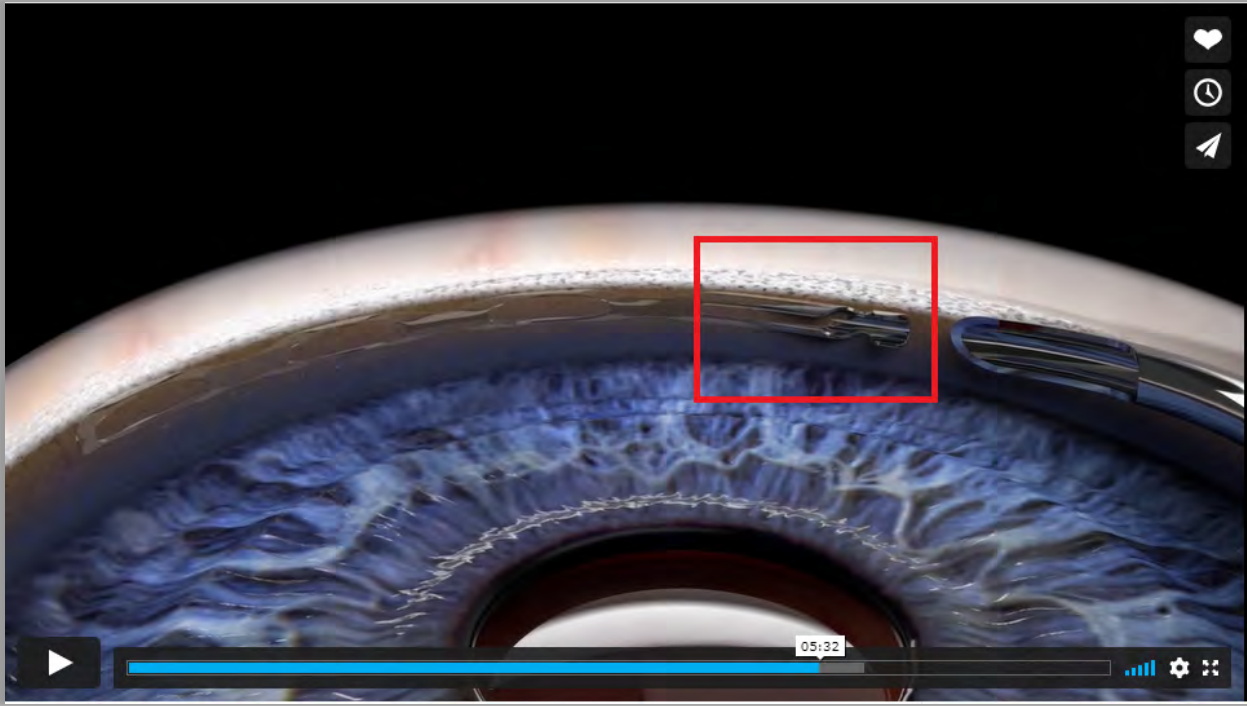
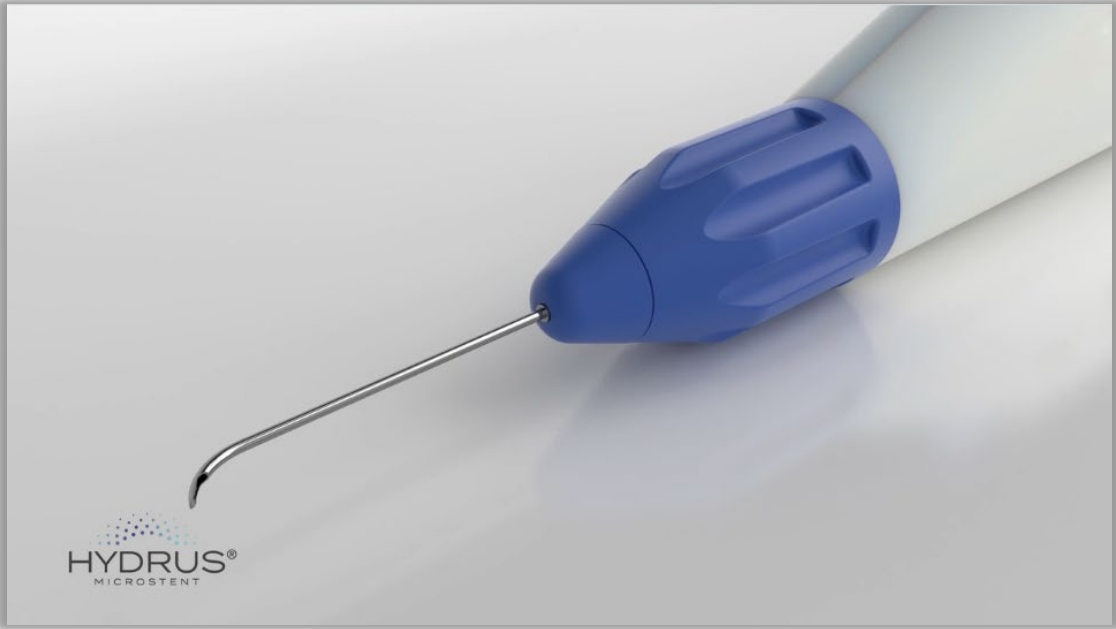
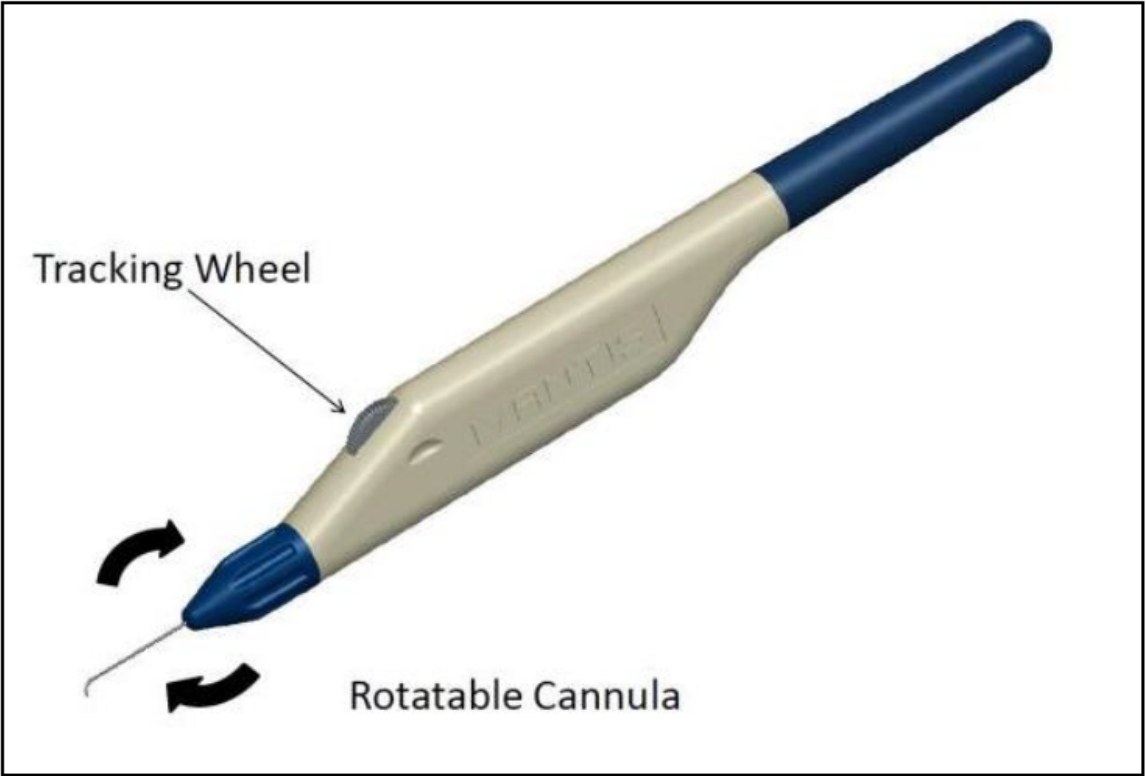
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="556 289 1795 990"></div> <p data-bbox="485 1052 850 1084">(Hydrus Animation at 5:32.)</p> <ul data-bbox="533 1128 1877 1234" style="list-style-type: none">• “Continue to advance the microstent until a physical stop is felt and the interlock releases the microstent. Verify that the inlet of the microstent is positioned in the anterior chamber.” (IFU at 7.)

EXHIBIT P

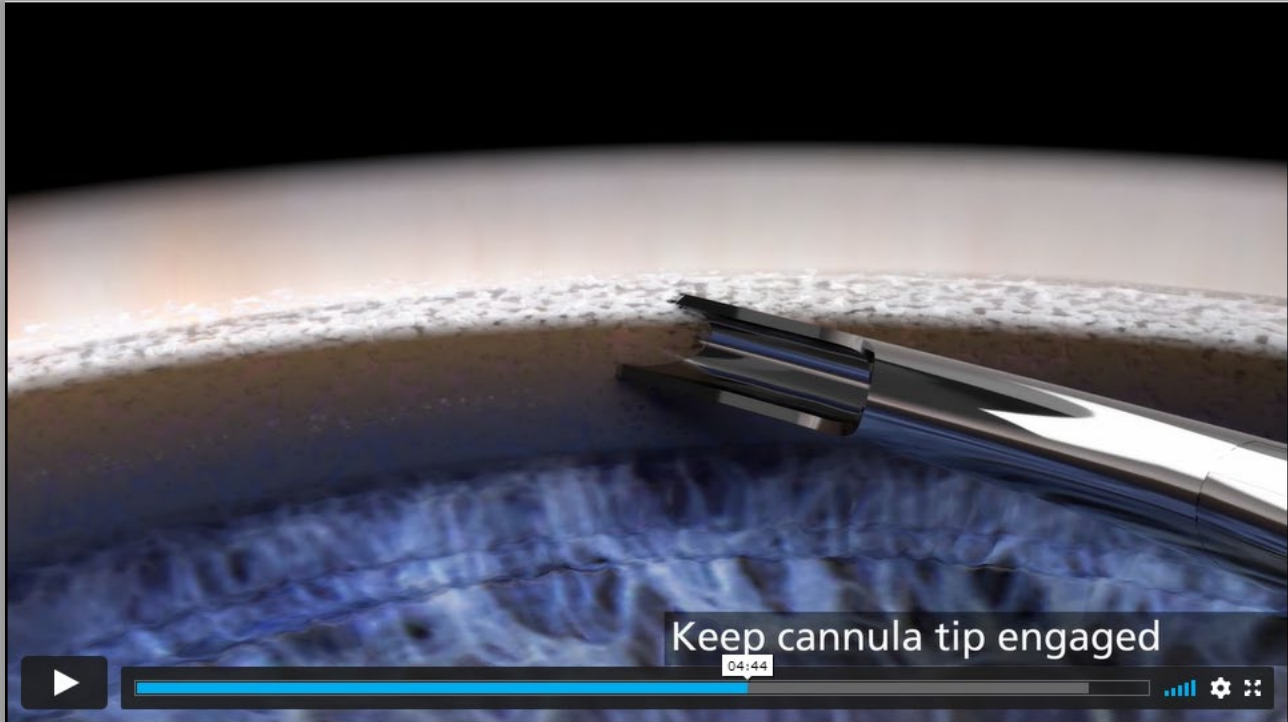
Exemplary Claim Chart of Hydrus® Microstent Against U.S. Patent No. 11,389,328 (“’328 Patent”)

Claim [Limitation]	Evidence of Infringement
<p>1[pre]: A method for reducing intraocular pressure in a patient using a support and an introducer comprising a cannula, comprising:</p>	<p>The procedure for implanting the Hydrus Microstent is a “method for reducing intraocular pressure”:</p> <ul style="list-style-type: none"> • “Ivantis, a company dedicated to the development of innovative solutions for glaucoma therapy brings you the Hydrus Microstent, a groundbreaking MIGS technology designed to relieve the high intraocular pressure of the eye that is common in patients with primary open angle glaucoma.” (“IM-00 16-1-2 Rev B OUS Hydrus Microstent Animation (Full)”, https://vimeo.com/510821860 (hereinafter “Hydrus Animation”) at 1:35 – 1:55.) • “The Hydrus Microstent is indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure (IOP) in adult patients with mild to moderate primary open-angle glaucoma (POAG).” (Hydrus Microstent Instructions for Use (hereinafter “IFU”), at 3.) <p>The Hydrus Microstent is a “support”:</p> <ul style="list-style-type: none"> • “The microstent (Figure 1) is composed of nitinol, a metal alloy of nickel (Ni) and titanium (Ti). Nitinol has been used extensively in a variety of implantable devices for its proven properties of flexibility, strength and biocompatibility. As a shape memory alloy, nitinol has super-elastic properties making it suitable as a support structure in Schlemm's canal. The implant is laser cut from nitinol tubing to a proprietary design with alternating “spines” for structural support and “windows” to provide outflow pathways for aqueous humor. After laser cutting, the shape of the implant is heat-set to a curvature that matches the curvature of Schlemm’s canal and is electro-polished to create a smooth biocompatible surface. The microstent is approximately 8mm in overall length with major and minor axes of 292µm and 185µm, respectively. The length and curvature of the implant are designed to occupy approximately 90° or 3 clock hours of Schlemm’s canal. The implant is designed to have adequate structural thickness to support the tissue of the canal while providing maximum

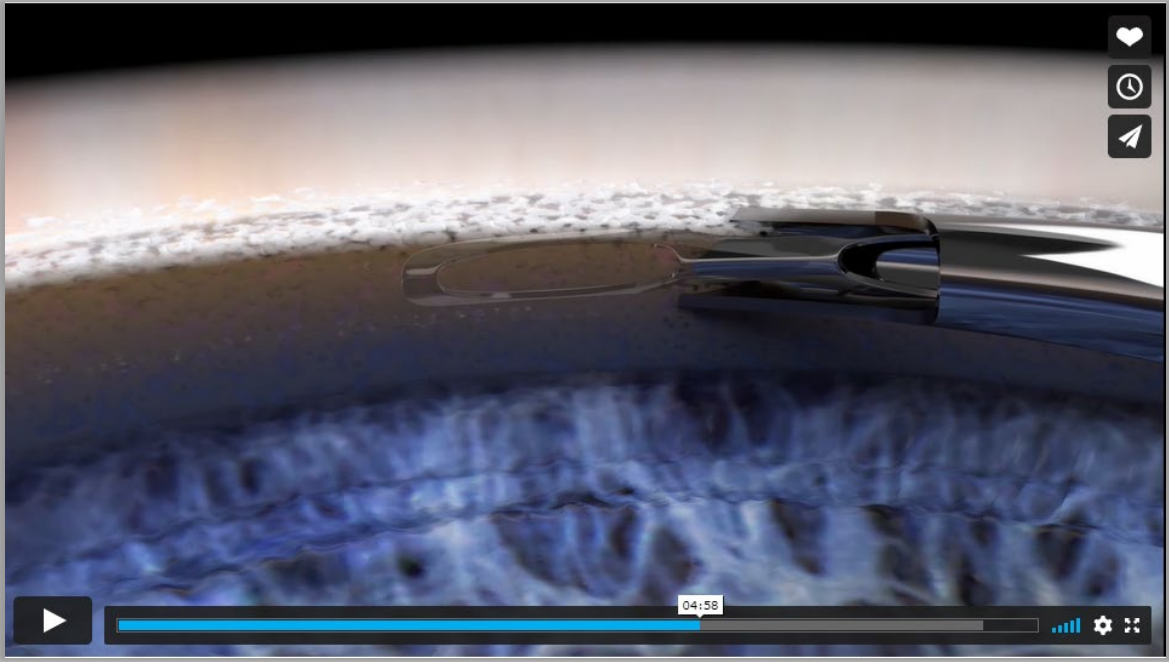
Claim [Limitation]	Evidence of Infringement
	<p data-bbox="674 233 1902 337">open flow areas through the canal, with the proximal portion of the implant exiting the canal through the trabecular meshwork to allow inflow of aqueous humor from the anterior chamber.” (IFU at 1.)</p> <p data-bbox="579 380 1640 412">The Hydrus Microstent is delivered using an “introducer comprising a cannula”:</p> <div data-bbox="688 467 1797 1092"></div> <p data-bbox="579 1146 947 1179">(Hydrus Animation at 3:57.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="625 248 1860 1159"><p data-bbox="869 1089 1604 1127">Figure 2: Hydrus Microstent Delivery System</p></div> <p data-bbox="579 1219 716 1256">(IFU at 2.)</p> <ul data-bbox="630 1295 1866 1365" style="list-style-type: none"><li data-bbox="630 1295 1866 1365">• “The microstent is implanted into the eye using a hand-held delivery system (Figure 2) that provides for delivery of the implant through a stainless steel cannula into the target site in the

Claim [Limitation]	Evidence of Infringement
	<p>eye. The delivery system was designed to provide smooth tracking and controlled delivery of the microstent into Schlemm's canal. The delivery system is an ergonomic design for use in either the right or left hand, allowing for surgeon individual preference and hand position. To accommodate a wide range of hand positions, a rotatable sleeve at the distal end allows positioning and alignment of the cannula by the surgeon to direct the implant into Schlemm's canal. The tracking wheel on the delivery system serves as the control mechanism to advance the implant into the canal or retract the implant into the cannula." (IFU at 2.)</p>
<p>1[a]: positioning a distal end of the cannula at or near Schlemm's canal, wherein the support is located in a lumen of the cannula; and</p>	<p>The procedure for implanting the Hydrus Microstent involves "positioning a distal end of the cannula at or near Schlemm's canal"</p> <ul style="list-style-type: none"> • "To deliver the microstent into Schlemm's canal, the cannula of the delivery system is inserted through a clear corneal incision (approximately 1.5 mm in length). The cannula tip is then advanced through the trabecular meshwork until it enters Schlemm's canal and the entry point into the meshwork is coincident with the end of the cannula bevel. The target tissue is visualized using a gonioscopic prism. After observing that the distal cannula tip is properly positioned through the trabecular meshwork into Schlemm's canal, the tracking wheel on the delivery system is used to advance and release the microstent." (IFU at 2-3 (emphasis added).)

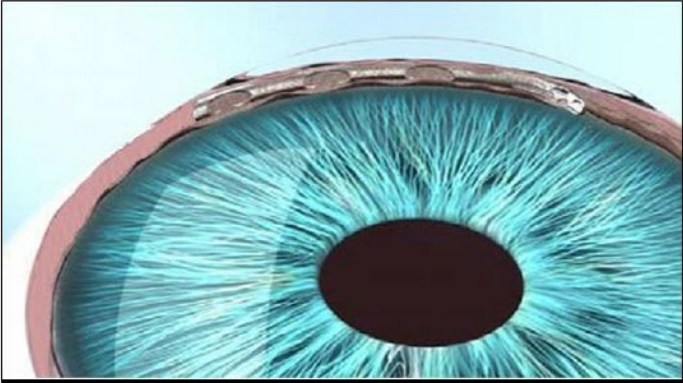
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="600 253 1881 971"></div> <p data-bbox="579 1036 945 1068">(Hydrus Animation at 4:44.)</p> <ul data-bbox="630 1110 1902 1328" style="list-style-type: none">• “The Hydrus cannula is inserted through a corneal incision at the temporal position and directed towards the trabecular meshwork where it is positioned parallel to Schlemm’s canal. Under gonioscopy, the beveled tip of the cannula should be tilted up approximately fifteen degrees, and then used to access Schlemm’s canal through the trabecular meshwork, just above the scleral spur. Once through the trabecular meshwork, hold the cannula steady with light contact against the back wall of Schlemm’s canal.” (Hydrus Animation at 4:05 – 4:40.)

Claim [Limitation]	Evidence of Infringement
	<ul style="list-style-type: none"> • “Begin to deliver the Hydrus by gently rolling the tracking wheel forward while keeping the cannula tip engaged. Continue to advance the Hydrus with a slow and steady motion while gently relaxing the upward and forward pressure on the cannula. The Hydrus highly flexible rounded frame design provides for a smooth passage into Schlemm’s canal. Observing the first window of the Hydrus as it enters Schlemm’s canal will provide verification that the device is being delivered properly. You’ll notice how the translucency of the trabecular meshwork causes the Hydrus to appear less shiny as it is delivered. Once satisfied with its position, the Hydrus is advanced until the microstent is released from the interlock. The Hydrus cannula is then removed from Schlemm’s canal and withdrawn from the eye.” (Hydrus Animation at 4:40 – 5:38.) <p>Furthermore, the Hydrus Microstent is “located in a lumen of the cannula,” the distal end of which is positioned at or near Schlemm’s canal:</p>


Claim [Limitation]	Evidence of Infringement
	<div data-bbox="604 248 1766 906"></div> <p data-bbox="579 963 945 995">(Hydrus Animation at 4:58.)</p> <ul data-bbox="630 1040 1892 1182" style="list-style-type: none">• “When the cannula tip is in the canal and the first window of the microstent is visible, align the cannula to be parallel with the iris. Continue to advance the microstent by rolling the wheel slowly. If resistance is felt, stop advancement, retract if necessary and readjust the position of the cannula.” (IFU at 7.) <p data-bbox="579 1222 957 1255"><i>See also</i> Claim 1[pre], above.</p>

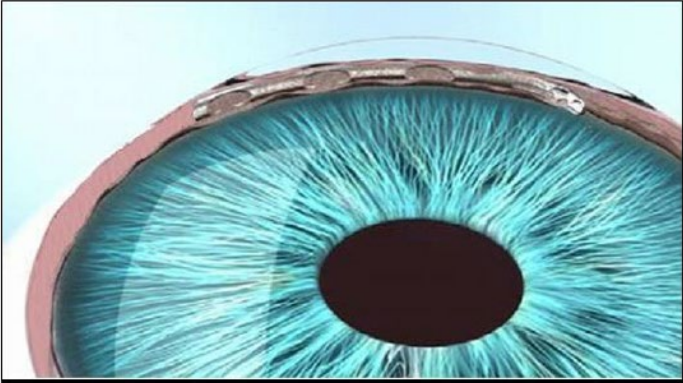
Claim [Limitation]	Evidence of Infringement
<p>1[b]: pushing the support distally out of the distal end of the cannula to insert the support circumferentially within Schlemm's canal,</p>	<p>The procedure for implanting the Hydrus Microstent involves “pushing the [Hydrus Microstent] distally out of the distal end of the cannula to insert the support circumferentially within Schlemm’s canal”:</p> <ul style="list-style-type: none"> • “To deliver the microstent into Schlemm’s canal, the cannula of the delivery system is inserted through a clear corneal incision (approximately 1.5 mm in length). The cannula tip is then advanced through the trabecular meshwork until it enters Schlemm’s canal and the entry point into the meshwork is coincident with the end of the cannula bevel. The target tissue is visualized using a gonioscopic prism. After observing that the distal cannula tip is properly positioned through the trabecular meshwork into Schlemm’s canal, the tracking wheel on the delivery system is used to advance and release the microstent.” (IFU at 2-3 (emphasis added).)

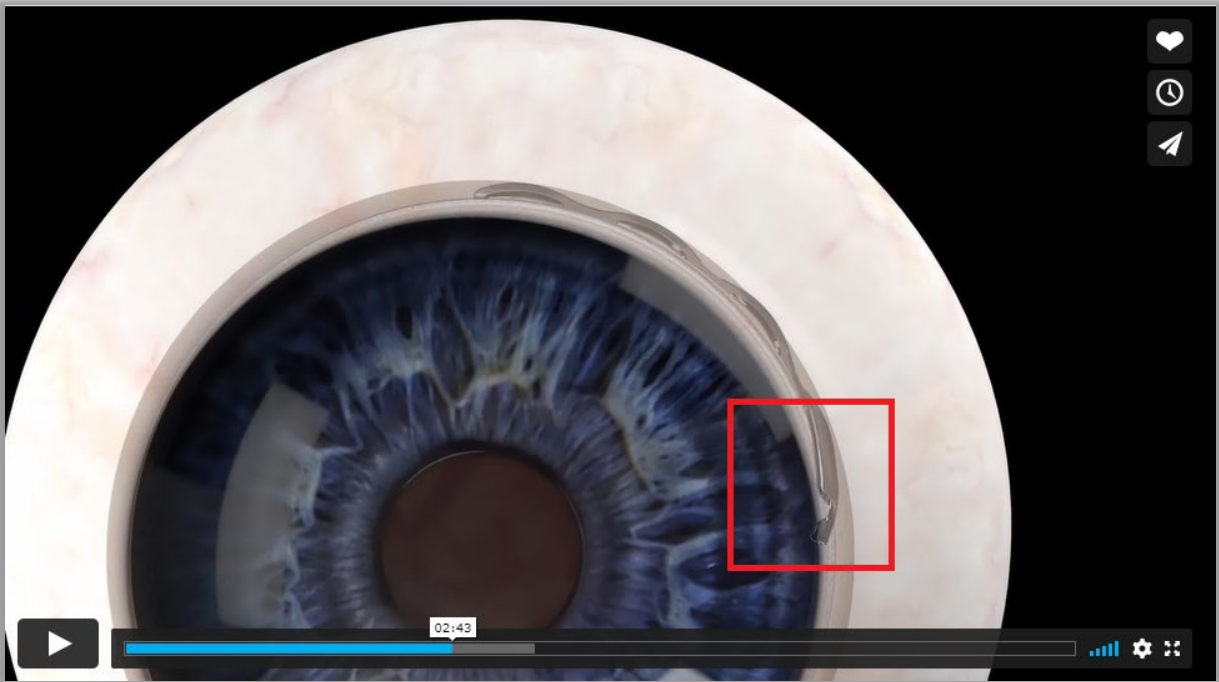
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="688 245 1793 721" data-label="Image"> </div> <p data-bbox="579 781 716 813">(IFU at 6.)</p> <ul data-bbox="630 857 1902 1146" style="list-style-type: none"> • “Pierce the trabecular meshwork by aiming the cannula tip at a slight angle anteriorly (approximately 15 degrees) toward the target. After piercing the TM, the cannula tip should slide gently into Schlemm’s canal. Care should be taken with cannula tip approach to fully incise the TM and position the cannula against the posterior wall of Schlemm’s canal. When the cannula tip is in the canal and the first window of the microstent is visible, align the cannula to be parallel with the iris. Continue to advance the microstent by rolling the wheel slowly. If resistance is felt, stop advancement, retract if necessary and readjust the position of the cannula.” (IFU at 7.)

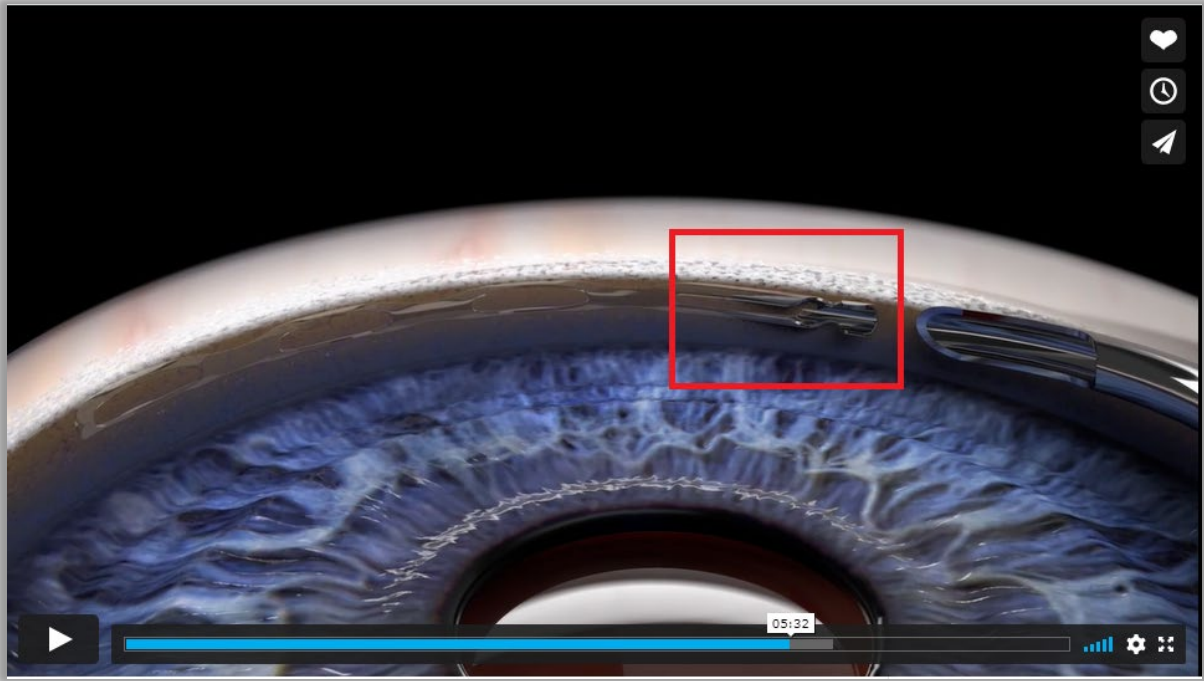
Claim [Limitation]	Evidence of Infringement
	<div data-bbox="640 248 1848 812">  <p data-bbox="661 699 1827 781">Figure 5: Microstent in Schlemm's Canal (Proximal end at right accessing aqueous humor from the anterior chamber)</p> </div> <p data-bbox="579 867 716 899">(IFU at 8.)</p> <p data-bbox="579 943 930 976"><i>See also</i> Claim 1[a], above.</p>
<p data-bbox="201 1055 558 1331">1[c]: wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's</p>	<p data-bbox="579 1055 1331 1088">The Hydrus Microstent “comprises an arcuate member”:</p>

Claim [Limitation]	Evidence of Infringement
<p>canal such that at least a portion of the arcuate member extends out of Schlemm's canal.</p>	<div data-bbox="588 243 1837 917"></div> <p>(Hydrus Animation at 6:36.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="590 245 1808 935"></div> <p data-bbox="579 992 947 1029">(Hydrus Animation at 6:44.)</p> <p data-bbox="579 1065 1902 1170">At least a portion of the Hydrus Microstent arcuate member “has a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm’s canal such that at least a portion of the arcuate member extends out of Schlemm’s canal”:</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="640 248 1848 812"><p data-bbox="661 699 1827 781"><i>Figure 5: Microstent in Schlemm's Canal</i> (Proximal end at right accessing aqueous humor from the anterior chamber)</p></div> <p data-bbox="577 867 716 902">(IFU at 8.)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="638 250 1850 927"></div> <p data-bbox="579 987 1325 1024">(Hydrus Animation at 2:43 (red box added for emphasis).)</p>

Claim [Limitation]	Evidence of Infringement
	<div data-bbox="646 250 1843 927"></div> <p data-bbox="579 987 945 1019">(Hydrus Animation at 5:32.)</p> <ul data-bbox="630 1062 1902 1170" style="list-style-type: none">• “Continue to advance the microstent until a physical stop is felt and the interlock releases the microstent. Verify that the inlet of the microstent is positioned in the anterior chamber.” (IFU at 7.)